NOSOCOMIAL INFECTION IN A PAEDIATRIC INTENSIVE CARE UNIT:

INCIDENCE, SURVEILLANCE AND SEQUELAE

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TITLE

Nosocomial infection in a Paediatric Intensive Care Unit: incidence, surveillance and sequelae.

'Ad sanitatem gradus est novisse morbum'.
(It is a step toward health to know the disease).

Erasmus 1465 - 1536

FORMAL DECLARATION

I declare that I have written the dissertation presented to the University of Edinburgh for the Degree of Doctor of Medicine; that it is based upon my own observations and that, except as indicated in the thesis, the data were collected, analyzed and interpreted by me. The work has not been submitted for any other degree or diploma.

UNIVERSITY OF EDINBURGH

ABSTRACT OF THESIS (Regulation 7.9)

This thesis describes a study of nosocomial infection which was undertaken in the Intensive Care Unit, the Hospital for Sick Children, Toronto, Canada and which reviewed prospectively 685 patients from July 1987 to February 1988. The first aim of the study was to document the incidence of nosocomial infection by site and clinical pathogen in this population and to report the use of a severity of illness score (PRISM) as a predictor of the population at risk of acquiring infection. The second aim was to report the incidence of both wound and non-wound nosocomial infection in the post operative cardiac surgery patients with a focus on operative procedure and patient status at the time of surgery. The third aim was to report the sensitivity and specificity of a novel system of infection surveillance, recently introduced. The final aim was to document some adverse effects of nosocomial infection and to undertake a crude costing study of intravenous antibiotic required for their treatment.

As an introduction, the relevant literature is reviewed and certain issues such as infection surveillance, severity of illness scoring and criteria for infection are discussed in some detail. Study methodology is presented and ethical issues are considered.

The study reports nosocomial infection rate of 7 infected patients per 100 patients admitted. As a percentage of the total, the most prevalent pathogentic organisms are: coagulase negative staphylococci (32%), Pseudomonas aeruginosa (23%), Candida species (20%) and Staphylococcus aureus (9%); the commonest sites of infection are: blood stream (36%), skin/eye drain site (22%); respiratory tract (16%); wound (15%) and urinary tract (9%). Severity of the underlying illness on admission, as measured by the PRISM scoring system, predicts a population at risk of developing nosocomial infection. Patients with admission PRISM scores of ≥ 10 are significantly more likely to acquire infection that those with scores <10 (10.8% vs 3.6%, $p < 0.001$) and this association holds through age, clinical speciality and length of stay. The sensitivity, specificity, positive and negative predictive values of a PRISM score ≥ 10 are 75%, 53%, 11% and 97% respectively.

In post operative cardiac surgery patients non-wound infections account for 72% of the total nosocomial infections. With regard to wound infection; the most prevalent pathogenic organisms vary depending on whether surgery is closed ie.non bypass (Staph. aureus and coagulase negative staphylococci) or open ie. bypass (coagulase negative staphylococci, P. aeruginosa, Candida species and Staph. aureus). Risk factors for the acquisition of infection relate to specific operative procedures and to surgical technique particularly the presence of an open sternotomy wound in the post operative period.

The system of infection surveillance recently introduced in the PICU (the Infection Control Sentinel Sheet; ICSS) compares favourably with daily bedside examination of patients plus daily review of in-patient charts. The ICSS, which requires only 20 minutes of surveillance time per day, detects 87% of nosocomially infected patients; 85% of infections at the three standard sites (blood, wound and urine); and 72% of infections at all of the 11 sites surveyed.

Certain adverse effects of nosocomial infection are reported to occur in up to 40% of infected patients. A crude costing study of intravenous antibiotic required for treatment of nosocomial infection suggests that the minimum cost was $Can 15,000 (approx £7,500).

In conclusion, following a resume of the results of the individual studies, areas, where future research efforts might be focussed, are identified.

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LIST OF ABBREVIATIONS USED IN THE TEXT

AIDS	Acquired immune deficiency syndrome
APACHE	Acute physiology and chronic health evaluation
ASD	Atrial septal defect
AVSD	Atrio-ventricular septal defect
BSO/CR	Bed-side observation/chart review
BT	Blalock-Taussig
CCS	Clinical Classification Scoring
CDC	Centre for Disease Control
CONS	Coagulase negative staphylococci
CPB	Cardiopulmonary bypass
CSF	Cerebrospinal fluid
CVL	Central venous line
DRG	Diagnosis Related Group
HSC	Hospital for Sick Children, Toronto, Canada
ICN	Infection Control Nurse
ICP	Infection Control Practitioner
ICP	Intracranial pressure
ICSS	Infection Control Sentinel Sheet
ICU	Intensive Care Unit
JCHA	Joint Committee on Hospital Accreditation
JP drain	Jackson Pratt drain
LA	Left atrium
NICU	Neonatal Intensive Care Unit
NIPR	Nosocomially infected patient ratio
NIR	Nosocomial infection ratio

NNIS	National Nosocomial Infection Survey
PA	Pulmonary artery
PD	Peritoneal dialysis
PICU	Paediatric Intensive Care Unit
PSI	Physiologic Stability Index
PRISM	**P**aediatric **RIS**k of **M**ortality
RA	Right atrium
RSV	Respiratory syncytial virus
SENIC	Study on the Efficacy of Nosocomial Infection Control
TISS	Therapeutic Intervention Scoring System
URTI	Upper respiratory tract infection
VSD	Ventricular septal defect

THE PURPOSE OF THIS THESIS

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It is essential to understand the epidemiology of nosocomial infection in the Paediatric Intensive Care Unit (PICU) and the underlying risk factors for its development, in order to elaborate effective intervention strategies and thereby reduce associated morbidity, mortality and patient care expenditure. If this aim is to be realized, an adequate paediatric data base must be available which should be developed by undertaking specific studies in infants and children rather than extrapolating from the results of studies performed in adults.

To date, the majority of reports in the PICU-related literature have solely addressed epidemic infection. Only a very few studies of endemic infection have been published and they have demonstrated considerable diversity in certain aspects of study methodology namely criteria for infection, definition of infection rates and infection surveillance. There have also been differences with respect to population characteristics; the severity of their underlying illness, their patterns of length of stay as well as efforts at prevention of infection. These variations make it difficult to draw conclusions from the results of individual studies and preclude comparisons of results between institutions.

In the past, attempts have been made to associate certain

underlying risk factors such as use of therapeutic devices, clinical specialty, length of stay and age with the subsequent acquisition of infection. Even though severity of underlying illness is probably the single most important factor determining the risk of acquiring infection in the critically ill subjects, to date, its role has not been defined in paediatric patients.

Commonly, cardiac surgical patients represent a significant proportion of the PICU population. Surveys of nosocomial infection in this group of patients have been confined to wound infection only; the incidence of non-wound infection has not been documented and infections have not been stratified either by surgical procedure or patient status at the time of surgery.

A novel system of nosocomial infection surveillance (the Infection Control Sentinel Sheet) has been developed by the Infection Control service for routine use in the Hospital for Sick Children, Toronto. The system has been applied in the PICU for more than a year; its specificity and sensitivity require evaluation in this clinical area.

In the critically ill child to quantify objectively the adverse effects of nosocomial infection is not a simple matter since associations of infection with either mortality or deterioration in clinical status or increased length of stay/increased patient care expenditure are all

subject to the confounding effects of multiple uncontrolled variables. To date, the adverse sequelae of nosocomial infection have not been formally studied in critically ill children and in the PICU the burden of illness resulting from nosocomial infection has not been addressed.

The work for this thesis was carried out in the Intensive Care Unit of the Hospital for Sick Children, Toronto, Canada. The aims of the thesis were as follows:-

1. To define the PICU population using a validated severity of illness scoring system (the PRISM system) as well as traditional demographic data.

2. To undertake daily surveillance of this population using bedside examination plus patient chart review and systematically record the incidence of nosocomial infection by site and organism, using clearly defined criteria for infection.

3. To report the use of the PRISM score as a predictor of the PICU population at risk of developing nosocomial infection.

4. To report the incidence of wound and non-wound nosocomial infection in the population of cardiac surgical patients with a focus on severity of illness and operative procedure.

5. To document the occurence of selected adverse effects of nosocomial infection in the PICU and undertake a crude costing study of antibiotic required as treatment for nosocomial infection.

6. To estimate the effectiveness and efficiency of a novel system of infection surveillance currently in routine use - The Infection Control Sentinel Sheet (ICSS).

CHAPTER 1

INTRODUCTION

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SUMMARY

In the following chapter I shall endeavour to provide an overview of nosocomial infection in the Paediatric Intensive Care Unit (PICU). The chapter opens with a discussion of nosocomial infection, as it occurs in paediatric patients in general, followed by a resume of the risk factors and exposures particularly associated with the acquisition of infection in the PICU. The related literature is then reviewed, the formal studies of nosocomial infection undertaken so far are discussed and their limitations are identified. Thereafter, the adverse sequelae of nosocomial infection, and the difficulties associated with their measurement, are considered. Finally, the features of an ideal system of nosocomial infection surveillance, suitable for routine use in the PICU, are propounded.

1.1 BACKGROUND

For many years it has been recognized that individuals are subject to increased risks of acquiring infection while in hospital and this infection has been variously referred to as cross infection, hospital-acquired infection and, more recently, nosocomial infection.

More than half a century ago, the problem of cross infection, and its control in children's hospitals, was the subject of debate at medical gatherings and in the medical press (Lancet 1933 [Leader]) (Glover 1934). In 1935, in one of the Milroy lectures delivered before the Royal College of Physicians in London, Dr. E. H. R. Harries, Medical Superintendent of London County Council, presented the results of an incidence study of cross infection, undertaken between October, 1933 and September, 1934, in the North Eastern Fever Hospital, London. During the study period there were 221 episodes of cross infection in 5712 admissions - a rate of 3.8 infections per 100 patients admitted. The commonest causes of cross infection were scarlet fever, diphtheria, whooping cough, chickenpox, measles and rubella although other infections such as impetigo, Sonne dysentery, otitis media and ringworm were observed. Souces of infection were classified as one of three - external to the hospital; within the hospital but external to the wards and; within the wards namely children inadvertently admitted in the incubation or prodromal

period of an acute infective condition or else unrecognized carriers among patients, staff or visitors. Dr Harries was fully aware of the undesirable sequelae of cross infection which he claimed was "the bane of staffs of children's and fever hospitals." There follows a short extract from his dissertation:

> "Upon the consequences of extraneous infection it is unnecessary to dwell. They may be perilous to the individual child; they are always, in some degree, detrimental to the hospital. Long detention, especially if the cause be some superimposed infective process, may result in that complex of physical and psychical deterioration known as hospitalism.
> From the administrative standpoint, if wards are encumbered by long stay patients or closed to new ones, the machinery of admission and discharge breaks down. The overhead charges remaining undiminished, the average cost of the patient treated rises. Equally important, the reputation of the individual institution or of institutions of its particular type inevitably, if insensibly, suffers."
>
> 1935

The ensuing fifty years have witnessed a fundamental change in the role of the children's hospital. Today, hospital admission for the management of the acute infections of childhood is seldom required and the 'fever hospital' has become obsolete. Meanwhile, advances in medical technology have produced a requirement for highly specialized forms of patient care and 'new' clinical disciplines such as neonatal and paediatric intensive care medicine have evolved. Simultaneously over the last twenty years, enormous progress has been made in the clinical discipline of infectious diseases, which has been matched by developments in sundry laboratory specialties such as

immunology and pharmacology. The human immune system and the pathophysiology of processes of infection are now well understood and, currently, physicians are aided by a battery of sophisticated diagnostic and therapeutic techniques. Immunization schedules offer protection against a variety of organisms and research continuous unabated in search of new vaccines particularly those effective against viral infection. With regard to pharmacology; the last decade has seen a veritable explosion in the number of antibacterial, antiviral and antifungal drugs available for therapeutic use. Meanwhile, newly developed agents which act through manipulation of the immune system, for example monoclonal antibody, are showing promise.

Certainly, from the infectious diseases standpoint, the latter half of this century has seen some spectacular advances. Nonetheless, it is true to say that, at the present time, nosocomial infection generates as much concern in children's hospitals as it did fifty years ago. The nosocomial infection rate for children in general paediatric wards (expressed as the number of infections per 100 patients admitted) is estimated to be between 2% and 5% (Wenzel 1976a) (Gardner 1972) (MMWR 1984) (Donowitz 1986b) (Roy 1962) (Cooper 1970) (Welliver 1984) (Exon 1976) (McNamara 1967). For additional information the reader is referred to Jarvis' excellent review: 'Epidemiology of nosocomial infections in pediatric patients' (Jarvis 1987),

in which he combines data from published reports between January 1970 and April 1986, with data from the Centers for Disease Control's National Nosocomial Infections Surveillance (NNIS) System (Jarvis 1983). (NNIS was established in 1970 and is the only continuous national source of data on nosocomial infections in the United States). Ford-Jones (1987) also addresses the special problems of nosocomial infection in paediatric patients in Prevention and Control of nosocomial Infections.

With further regard to nosocomial infection in children, two significant statements can be made. Firstly, in recent years it has become clear that within any hospital it is critical care units which constitute the largest identifiable source of infection (Donowitz 1982) (Caplan 1981). Nosocomial infection rates in these units may be in excess of 20% (Wenzel 1976a) (Daschner 1982) (Kollish 1982) and critical care unit patients have nosocomial infection rates that are at least two to five times higher than those in the general wards. (Donowitz 1982) (Chandrasekar 1986) (Daschner 1982) (Massanari 1986) (Wenzel 1983). Patients in intensive care units are particularly vulnerable to primary bacteraemias, pneumonias and intra-abdominal infections. Infection is the most frequent cause of death - directly or indirectly - in patients who survive major trauma or full thickness burns and is the most common identified cause of multiple-organ failure. (Fry 1980) (Pin 1983) (Marshall 1983).

Secondly, as a general statement, the severity of illness of hospitalized infants and children is increasing, reflecting advances in technology and new approaches to patient care. For example: techniques such as organ transplantation and cytotoxic therapy produce large numbers of hospitalized, immuno-compromised patients; extremely complex cardiac surgical procedures are commonly performed on high risk patients - in modern day surgical management there are several indications for definitive cardiac surgery in the first few days or weeks of life, for example, the arterial switch procedure (Jatene 1976). Not surprisingly, the last decade has seen a significant increase in both the number and complexity of Paediatric Intensive Care Units (PICUs) designed to deliver optimal care to critically ill children and currently paediatric intensive care medicine is a rapidly developing field.

It is essential to understand the epidemiology of nosocomial infection in the PICU. Awareness of features such as the origin of infection, outcome status and the predominant sites and pathogens implicated may assist institutions in developing effective intervention strategies and reducing PICU related morbidity, mortality and financial cost. A better appreciation of the risk factors which predispose to infection may guide allocation of resources in infection control and focus research efforts. Furthermore, data from individual centres provide a yard stick against which other hospitals may gauge their

own infection rates for quality assurance purposes. To achieve these aims, an adequate paedatric data base must be developed and to do so specific studies must be undertaken in infants and children rather than extrapolating from the results of studies performed in adults or neonates.

So far, nosocomial infection in the PICU has been described relatively infrequently hence very little by way of a data base exists. In the literature only four formal studies of endemic infection have been published. (Welliver 1984) (Donowitz 1986b) (Brown 1987) (Milliken 1988) and in these reports infection rates range from 2.5 infections per 100 patients admitted. (Milliken 1988) to 13 infections per 100 patients admitted. (Donowitz 1986b). Studies have displayed considerable diversity in methodology and consequently the varying incidences of infection and the diverse proportional frequencies of infection by site and pathogen are somewhat difficult to interpret.

1.2 RISK FACTORS ASSOCIATED WITH NOSOCOMIAL INFECTION IN THE PICU

Patients admitted to the PICU are recognized to have an increased risk of acquiring infection for many reasons. (Holzman 1981) (Welliver 1984). Infections can occur in almost every organ system and are almost exclusively associated with some type of invasive monitoring or life-support system. Disease processes may compromise host defences as in cases of malignancy or burns, while cellular immunity may be depressed in the patient whose nutrition is less than optimal. (Edelman 1973) (Scrimshaw 1970). In neonates the immune system may be immature with deficits in both the mobility and the bactericidal activity of poly-morphonuclear leucocytes, particularly during stress. (Klein 1977) (US DHEW Publication 1975) (Yu 1974).

Children under two years of age have difficulty responding to polysaccharide antigen (Anderson 1977) (Cowan 1978) (Peltola 1977) and are particularly susceptible to infection with encapsulated organisms. This age group is also vulnerable to infection with viruses and it is noteworthy that both epidemiological and experimental evidence support the hypothesis that primary viral infection increases host susceptibility to secondary bacterial, fungal and protozoal infection. (Mills 1984).

Multiple operations and invasive procedures, both

therapeutic and diagnostic, may disrupt the integument or other host defences. Tracheal intubation provides a conduit which bypasses the normal host defence mechanisms of the upper airway, interferes with ciliary function and permits the passage of organisms from the supraglottic flora directly down into the trachea. Colonization of the airway occurs in virtually all patients in whom an artificial airway has been in place for more than 72 hours (Boysen 1979) though its significance is controversial. It has been suggested that most cases of nosocomial pneumonia are caused by aspiration of oral, pharyngeal or gastric contents (Clenenden 1985) and that such aspiration occurs in 70% to 80% of intubated neonates and children in whom the use of uncuffed endotracheal tubes is indicated. (Browning 1983) (Goodwin 1985).

Several reports have described a concordance between the bacteria found in stomach/nasopharyngeal contents, and those recovered from the trachea. (Atherton 1978) (de Moulin 1982) (Hillman 1982) (Swift 1984). It is assumed that organisms appear in the stomach contents by retrograde spread from the intestine, though it is possible that organisms from the mouth pass through the nasopharynx and are swallowed to join gastric contents. Also, it should be noted that retrograde colonization of the pharynx from the stomach is an important, alternative route of colonization. (Goularte 1986). Once in the stomach, the survival of organisms is encouraged by the use of antacids

and H_2 receptor antagonists which increase gastric pH. The stomach is normally sterile at an acid pH of 1 due to the potent bactericidal activity of hydrochloric acid. (Garrod 1939). Gastric colonization with gram negative bacilli may increase from zero at an acid pH of 1 to more than 100 million/mL at a pH of 6. (Donowitz 1986c) (Daschner 1988) (Goularte 1986).

Purulent otitis media and sinusitis are associated with mechanical ventilation, especially when a nasotracheal or nasogastric tube is present. Otitis media, which is usually preceded by middle ear effusion, has been described in PICU patients (Persico 1985). Sinusitis, which is usually preceded by purulent nasal discharge has been reported in adult ICU patients (Deutschman 1986) (Kronberg 1985) but, to date, no cases have been described in the PICU.

Urethral catheters predispose to nosocomial infection, as a result of contamination of the catheter or drainage system by the hands of nursing and medical personnel (Schaberg 1976). Up to one third of catheterised children may develop urinary tract infection. (Causey 1981). The risk of infection following a single in and out bladder catheterization is estimated to be between 1% and 2% . (Kunin 1966).

Invasive monitoring of intracranial pressure (ICP) is

indicated in the management of several disease states. (Moss 1979) (Rosner 1976). Central nervous system infection has been shown to occur in up to 27% of patients who have ICP monitoring devices (Mayhall 1984) though in children, the risk of infection has been reported to decrease after the sixth day of ICP monitoring. (Kanter 1985).

Colonization of vascular catheters and needles, sited both intravenously and intra-arterially, constitutes another serious source of nosocomial infection, commonly with organisms of skin flora (Maki 1973) (Crossley 1972) (Peter 1972) (Collins 1968) (Fuchs 1971) (Band 1979) (Adams 1980). The risk of colonization increases with duration of catheter use, method of catheter introduction, and type of catheter material used. Polyethylene catheters and steel needles tend to have a lower risk of colonization than plastic catheters, and the incidence of colonization in plastic catheters increases dramatically after 48 hours of placement. (Maki 1973). Colonization of central venous catheters and associated sepsis occurs in up to 27% of adult patients and correlates with duration of placement and the use of catheters for blood withdrawal. Candida and other fungi may be responsible for more than half of these infective episodes. (Maki 1973).

The risk of infection is greatest with pulmonary artery flotation (Swan-Ganz) catheters because of the need to

repeatedly withdraw blood samples and inject saline solution for determination of cardiac output. Studies have demonstrated that approximately one third of pulmonary artery catheter tips were colonized at the time of removal, though actual sepsis related to this occurred much less frequently (2 out of 92 patients). (Elliott 1979) (Luc 1979). Septic endocarditis (due to staphylococcus aureus) and aseptic vegetative endocarditis have been reported, rarely, as complications of Swan-Ganz catheter use. (Greene 1973, 1975) (Pace 1975).

In the PICU, the risk of procedure-related infections is further increased by the fact that life-saving interventions may be performed in an emergency situation with compromise of the usual aseptic technique. Other risk factors for infection may be identified: these patients are exposed to large numbers of hospital personnel; they reside in what is frequently the most crowded location within the institution and they often have prolonged stays. Intensive antiobiotic therapy, used in most critical care units, distorts patients' microflora and fosters colonization - and ultimately, infection with multiply resistant organisms and with yeasts such as Candida. (Finland 1970) (Pollack 1972) (Weinstein 1980, 1986) (Sanders 1983) (McGowan 1983).

Infants and children in the PICU are critically ill and it is suspected that in such patients the severity of

underlying illness is probably the single most important factor determining the risk of acquiring infection and its outcome. To date, studies investigating the role of severity of illness as a risk factor for nosocomial infection have been confined to critically ill adults and neonates. Results have been somewhat variable.

In 1978 Britt et al carried out a prospective study in adult medical patients and determined that the severity of underlying disease at the time of admission indicated patients at unusual risk of nosocomial infection. These workers used the system of severity of illness scoring devised by McCabe and Jackson in 1962 (section 2.3.1) which defined underlying illness as either "fatal", "ultimately fatal" or "non fatal". The nosocomial infection rate was 23.6% in patients with fatal underlying disease, 9.6% in those with ultimately fatal disease and 2.1% in those with non fatal disease.

More recently Craven et al (1988) prospectively studied over 1,300 adult medical and surgical ICU patients using the APACHE 1 score (section 2.3.6) to define severity of illness. This group of workers identified 23 variables which were univariately associated with the development of nosocomial infection (and which included severity of illness score). The technique of stepwise logistic regression analysis was then implemented to adjust for the confounding effect of different variables. Following this

manoeuvre, severity of illness score did not remain significant as a predictor of nosocomial infection though invasive devices did remain significant. Goldmann (1983) suggested that invasive devices were at least as important as underlying disease severity in determining susceptibility to infection in neonates though studies in the NICU are somewhat problematic since no accurate, reproducible system exists for scoring severity of illness in neonates. It should be noted that the use of invasive devices may in fact be a marker for patients with more severe underlying disease.

With regard to the PICU; nosocomial infections have been analyzed most frequently in terms of clinical specialty (Brown 1987), (Donowitz 1986b) (Welliver 1984) and, to a lesser extent, therapeutic interventions and devices. (Milliken 1988). In paediatric patients severity of illness has not been measured and the role of severity of illness as a risk factor for the development of nosocomial infection has not been defined. To control for severity of illness in the critically ill child requires quantitative and unbiased methods which, to be practicable, must be sufficiently easy to apply that dozens of admissions per month can be scored. Two systems for quantifying severity of illness in PICU patients have been validated - the Physiologic Stability Index (PSI) (Yeh 1984) (Pollack 1987a), and its modification the Paediatric Risk of

Mortality (PRISM) (Pollack 1988). Severity of illness scoring is reviewed more extensively in Chapter 2.3.

1.3 REPORTED INCIDENCE OF NOSOCOMIAL INFECTION IN THE PICU

Nosocomial infection in the PICU has been addressed infrequently and one reason for this may be the relatively small number of specialized PICUs available for study. In comparison, nosocomial infection in the Neonatal Intensive Care Unit (NICU) has been well described, (Hemming 1976) (Goldmann 1981a, 1981b) (Daschner 1983) (Hoogkamp-Korstanje 1982) (Brown 1985) (Jarvis 1987) (Maguire 1981) (LaGamma 1983) (Hall 1979) (Johnson 1984) (Munson 1982) (Baley 1984) (Anday 1985) and on occasion data from the NICU has been presented as PICU data (Massanari 1986). Likewise, there is a large pool of information relating to nosocomial infection in adult Intensive Care Units (Wenzel 1983) (Donowitz 1982) (Chandrasekar 1986) (Brown 1985) (Daschner 1982) (Northey 1974) (Preston 1981) (Caplan 1979) (Thorp 1979). Unfortunately, inferences concerning the PICU cannot be made from any of these data since it appears that infections acquired in these critical care areas differ substantially from infections acquired in the PICU in their incidence, character and morbidity (Jarvis 1983).

Pathogens which cause nosocomial infections may be either endogenous or exogenous. Endogenous pathogens are organisms which are part of the normal flora of patients and which under a variety of conditions, such as alteration of the host's physical, immunologic or microbiologic barriers, invade the host and become pathogenic.

Exogenous pathogens are organisms which are acquired from the external environment such as the PICU surroundings or from exposures e.g. invasive devices, clinical personnel.

In the main, nosocomial infection is transmitted by three routes. Transmission by common vehicles, such as water or compressed air supply (Bjerring 1987), may occur, although infrequently, and is usually confined to outbreaks. Airborne transmission, especially by droplets, is more common and includes transmission of viral infections. By far, the commonest route of transmission of nosocomial infection involves direct contact. Transmission via contact with contaminated medical equipment may occur and may involve urine collection receptacles (Schaberg 1976) (Rutala 1981); respiratory therapy equipment (Arnow 1982) (Gervich 1985) (Mehtar 1986); chamber domes or transducers used for haemodynamic monitoring (Weinstein 1976) (Donowitz 1979) (Pien 1986); dialysis machines (Favero 1974) (Berkelman 1982); or fibre-optic endoscopes (Schliessler 1980) and bronchoscopes (Webb 1975). However, the single most important route of infection involves contact with the hands of critical care unit staff, and handwashing has been repeatedly described as the major means of its interruption. (Donowitz 1987) (Mortimer 1962) (Albert 1981) (Steere 1975) (Larson 1988) (Reybrouck 1983). It is emphasized that the hands of personnel serve not only as a passive vehicle for the nosocomial transmission of organisms, but may actually constitute a reservoir for

their active multiplication. (Knittle 1975).

Nosocomial infections may be divided, somewhat arbitrarily, into epidemic infections, endemic infections, pseudo-infections and deliberate infections; to date it is epidemic nosocomial disease which has been most commonly reported. An epidemic is defined as 'an unusual, statistically significant increase in the incidence of a particular disease, usually occurring during a brief interval in a single patient population, and often due to a single microbial strain'. The critical care unit is a particularly favourable environment for the occurrence of epidemic nosocomial infection - particularly with antibiotic resistant pathogens. (Wenzel 1983) (Maki 1981). The somewhat diverse nature of epidemic infection in the PICU is illustrated by the following review of some cases selected from the literature. In addition the interesting, but rather uncommon, entities of pseudo-infection and deliberate infection will be considered.

In 1984 Gardner observed colonization of single dose vials of 0.45% saline (used for tracheal irrigation) with the organism Pseudomonas pickettii and reported a colonization rate of 31% during a three week period. In 1972 Morehead documented the epidemiology of epidemic pseudomonas infection in the PICU of the Children's Medical Centre, Dallas and in 1983, in the same unit, Anderson described an outbreak of infection with gentamicin resistant

Enterobacter cloacae. Hilton (1983) described a cluster of 10 eye infections which occurred in a mixed group of paediatric and adult intensive care unit patients, and which were due to dispersion of bacteria during suction of endotracheal tubes.

Bacteria and viruses may contaminate both blood products and medical equipment. A case of Serratia marcescens septic shock has been described in a ten year old PICU patient following transfusion with infected platelets. (Van Lierde 1985). Meanwhile, Fisher in 1981 and Noble in 1984 described clusters of bacteraemia due to contamination of pressure transducers with Pseudomonas maltophilia.

Sporadic nosocomial viral disease in the PICU has been reported by Krasinski (1985) who described upper respiratory tract infection with particular reference to Respiratory Syncytial Virus (RSV), and by Adams (1981) who described herpes simplex infection affecting both patients and nursing staff in a PICU.

Pseudobacteraemia has been demonstrated most commonly in patients undergoing coagulation studies. Citrated anticoagulant tubes have been shown to be contaminated with both Pseudomonas fluorescens (Simor 1985) and with Ewingella americana (Anderson 1985). When blood culture and coagulation studies are performed simultaneously, innoculation of the coagulation tube first (because it

requires a precise amount of blood) may result in contamination of the blood culture bottle and a spurious diagnosis of bacteraemia. While pseudoinfections originating in this manner are not unique to paediatric patients, they may occur more frequently in this group because of technical difficulties associated with blood sampling.

Factitious illness in children, which has been induced by adults, is a recognised entity, albeit one which is reported infrequently. Polle syndrome has been suggested as the preferred term for this child abuse variant of Munchausen syndrome (also known as Munchausen by proxy).

Deliberate infection of hospitalized children (usually by the mother) has been reported by Kohl in 1978, by Pickering in 1981, by Hodge in 1982 and by Liston in 1983. In clinical presentation cases resemble organic illness occurring in association with polymicrobial bacteraemia. However, despite extensive investigation no underlying disease can be substantiated. To date no cases of this condition have been reported in the PICU.

Footnote
Polle, who died at the age of one year, was the sole son of Baron Von Munchausen. It is thought that the Baron may have contributed to the child's early demise. (Burman 1977).

It may be concluded that sporadic nosocomial disease has been fairly well described and, indeed, most of our understanding of nosocomial infection in the PICU is based on studies of epidemics. It is apparent however, from clinical practice, that the majority of nosocomial infections occurring in this area are endemic in nature and have no single or predominant cause. Despite this fact the current literature contains reports from only four PICUs in which the epidemiology of endemic nosocomial infection has been systematically studied; these are summarised in Table 1. Each study will be reviewed with particular reference to the estimated nosocomial infection rate and the observed distribution of infections by site, pathogen and clinical speciality.

Table 1 Reported PICU Nosocomial Infection Ratios.

Hospital	#PICU Beds	Infection Ratio*	Surveillance Method	Surveillance Duration
Children's Hospital of Buffalo	18	11.0	Review of:- Nursing Kardex; all lab reports; medical record discharges.	12 months
Bay State Medical Center Springfield Mass., USA.	6	6.2	Ward survey	3 years
University of Virginia Hospital	6	13.7	Review of nursing twice weekly to high risk patients for chart review	12 months
Hospital for Sick Children Toronto	18	2.6[a] 6.1[b]	Review of:- nursing kardex- twice weekly; lab reports daily 5 days/week.	30 months

* number of infections per 100 patients admitted or discharged.

[a] all PICU patients

[b] patients remaining in PICU for 72 hours or more.

In Buffalo Children's Hospital, Welliver studied the epidemiology of nosocomial infection occurring throughout the hospital including the PICU. The study expressed the incidence of nosocomial infection as "attack rates" (number of infections / 100 patients discharged), and recorded a rate of 11% in the 18 bedded PICU over a 1 year period (1980 - 1981). No information was available with regard to the distribution of PICU infection by site, clinical speciality or pathogen. (Welliver 1984).

Brown et al in Baystate Medical Centre Massachusetts expressed the incidence of nosocomial infection as an infection rate (number of infections/number of ICU admissions x 100) and reported a PICU acquired infection rate of 6% in 965 children admitted to their six bedded PICU during a two year period (1982-1984). This study differed slightly from the others since it described all infections i.e. community acquired and PICU acquired. Staph. aureus accounted for 20% of infections, Klebsiella-Enterobacter-Serratia for 18.3% of infections and E.Coli for 15% of infections. There was no information regarding the distribution by site or clinical speciality of those infections specifically acquired in the PICU, though this information was available with respect to the total number of infections (PICU acquired plus community acquired). (Brown 1987).

Donowitz in the University of Virginia, expressed the

incidence of nosocomial infection as an infection rate (number of infections/100 patients admitted) and reported a rate of 13.7% during a 1 year period (1982-1983) in a 6 bedded PICU. The clinical specialities with the highest infection rates were paediatric surgery (18.6% of infections), thoracic/cardiovascular surgery (15.5% of infections) and plastic surgery (13.2% of infections). Site specific infection rates, expressed as a percentage of total infections were detailed for: lung infection (21% of infections), urinary tract infection (15%), postoperative wound infection (10%) and blood stream infection (8%). Specific pathogens were identified for bloodstream infections only; the organisms identified most frequently were Staph. epidermidis, Staph. aureus, Serratia liquifaciens, and Escherichia Coli. (Donowitz 1986b).

In the Hospital for Sick Children, Toronto, Milliken et al reviewed nosocomial infections occurring in 3,220 PICU patients over a period of 30 months (1983-1985). This group expressed the incidence of nosocomial infection as a nosocomial infection ratio (number of patients acquiring one or more infections divided by the total number of patients admitted x 100). They reported infection ratios of 2.6% for all patients admitted to the PICU and 6.1% for those patients who remained in the PICU for a minimum of 72 hours. The most frequent sites of infection were, in descending order:- bloodstream (40% of infections), lower respiratory tract (15% of infections), gastrointestinal and

urinary tract, skin and eye, post operative wound and upper respiratory tract, peritoneal fluid. Clinical speciality specific nosocomial infection ratios were, in descending order:- neurosurgery (13.1% of infections) paediatric surgery (11.2%), neurology (9.1%), renal (7.4%), ENT (5.8%), general paediatrics (5.7%), cardiovascular surgery (4.7%), plastic surgery (3.6%). The most common pathogens isolated were gram positive cocci (42% of infections) with coagulase-negative isolates accounting for 22% of infections. Pseudomonas aeruginosa was the second most common bacterial isolate causing nearly 20% of infections. The relative frequency of virus infection was low (5.7% of infections). (Milliken 1988).

It is noteworthy that, during their respective periods of study, no institution observed an epidemic of infection arising within the PICU and no occurrences of pseudo-infection or deliberate infection were reported.

In the multidisciplinary PICU, patients from the cardiac surgery service frequently constitute a significant proportion of the patient population. Our own experience is that some 40% of admissions are postoperative cardiac surgery patients. Nonetheless, the epidemiology of nosocomial infection in this particular group has been poorly documented and to date studies have reported the incidence of wound infection only.

During a 12 month study period involving 6,775 procedures, Edwards (1983) identified 9 children (0.1%) with median sternotomy wound infections which included 3 children with mediastinitis. Elsewhere, Culliford et al identified wound infections in 0.4% of 227 children undergoing median sternotomy, though patients with mediastinitis were not specifically identified (Culliford 1976). To date no study has stratified cardiac wound infection by operative procedure or by the status of the patient at the time of surgery. Furthermore, despite the increasing use of complex, invasive monitoring devices, the incidence of non-wound nosocomial infections in paediatric cardiac surgical patients has not been documented.

1.4 LIMITATIONS OF PREVIOUS STUDIES OF NOSOCOMIAL INFECTION IN THE PICU

Formal studies of endemic nosocomial infection, so far undertaken in the PICU, have certain limitations which merit further discussion. The studies present diversity in both purpose and method and at times precise details of methodology are not made available. These differences limit the ability to make generalizations from results of individual studies and also hamper comparisons of results either between institutions or within the same institution over time. The methodologic areas where there have been substantial differences include: definitions of rates of infection, criteria for infection, and methods of

surveillance (case finding). Studies also differ with respect to the characteristics of the population under review - the severity of their underlying disease; patterns of length of stay and efforts at prevention of infection. All of these features may change over time and geographic setting.

At this juncture, I do not intend to discuss particular issues of methodology further but Chaper 2 is devoted to detailed review of certain aspects of study namely surveillance of infection, criteria for infection, definition of rates of infection and severity of illness scoring.

1.5 ADVERSE SEQUELAE OF NOSOCOMIAL INFECTION IN THE PICU

When one considers the adverse effects of nosocomial infection ideally, all outcomes should be measured: death, disease, disability, discomfort and dissatisfaction. Every aspect of patient well being, physical, social and emotional, should be considered as well as the attributable cost of infection to patients, parents and health care systems. There are no reports from paediatric intensive care units which describe the adverse sequelae of nosocomial infection and it is unclear what 'burden of illness' nosocomial infection creates in this clinical environment. To establish a causal association between nosocomial infection and a particular adverse outcome

presents formidable difficulties because of the confounding effects of multiple uncontrolled variables. I shall now review certain statistical issues which may complicate the analysis of multiple variables in hospital epidemiology (namely confounders and effect modifiers) and the various techniques which have evolved to offset them.

1.5.1 Statistical Issues

1.5.1.1 Confounders and effect modifiers

Any study which involves epidemiological comparisons has two primary variables - an exposure and an outcome. A third variable, which is neither the exposure nor the outcome, can distort the apparent effect of the exposure in determining the outcome. Several factors or determinants acting jointly are almost invariably responsible for any single outcome in hospital epidemiology. If one is interested in the causative effect of just one of these factors and investigates only one of these risk indicators without considering the contributory effects of the others, then the crude measure of the association will probably be distorted by confounding. In simple terms, a confounding variable may be thought of as an alternative cause to the determinant or risk factor under study whose effect is mixed with that of the study variable. In simple terms an effect modifier is a third variable, neither the exposure nor the outcome, which modifies the effect of a specified

exposure of an outcome. A confounder actually distorts a comparison and, if not corrected, confounding will produce a wrong answer whereas an effect modifier (provided it is not also a confounder) does not distort a comparison, but provides alternative information about the exposure and outcome with respect to the third variable.

Historically, the problem of a confounder distorting a hospital epidemiological study was first observed by McCabe and Jackson in their investigation of the effects of bacteraemia with gram negative bacilli (see chapter 2, section 2.3.1). In this study the species of infection bacteria was the exposure, mortality was the outcome and the third extraneous variable having a major influence on mortality turned out to be severity of the underlying disease. Following this study it was recognized that correction for the distorting effect of differing degrees of health or illness was the major analytic problem facing hospital epidemiologists.

1.5.1.2 Analysis of multiple variables - statistical techniques

It is usually impractical to conduct planned experiments in a hospital population with a concurrent comparison population that only differs by one variable, because nature seldom changes only one variable at a time. Methods have been devised by biostatisticians for analyzing data

containing information on multiple variables; some of these statistical techniques are briefly reviewed.

Risk Ratio

The risk ratio is actually the ratio of two probabilities; the probability of the outcome among the exposed, over the probability of the outcome in the unexposed (Cornfield 1951). The risk ratio has an immediate clinical interpretation. If the risk of the outcome is the same in both the exposed and the unexposed groups, the risk ratio will be unity indicating no effect. A risk ratio of 2.0 means the exposed are twice as likely as the unexposed to have the outcome in question. A risk ratio of 0.5 indicates the exposed are half as likely as the unexposed to have the outcome. A risk ratio of less than unity suggests prevention. The terms 'risk ratio' and 'relative risk' may be used interchangeably.

Stepwise Logistic Regression Analysis

Stepwise logistic regression models allow simultaneous control of multiple factors. Models are commercially available (Statistical Analysis Systems Inc. Carey, NC).

Mantel-Haenszel Procedure

Cochran, Mantel and Haenszel have developed methods for

summarizing discrete data in multiple four-fold tables, or multiple strata, in direct analogy with generalized methods of analysis of variance. (Cochran 1954) (Mantel 1959) (Mantel 1963). These developments allow summary statistics (chi or chi-square) and summary estimates of risk ratio to be produced over multiple strata. They are well summarized in recent textbooks. (Kleinbaum 1982) (Rothman 1986). The Mantel-Haenszel procedure is the strategyf implemented in this study to analyze data containing information on multiple variables.

1.5.2 Nosocomial Infection and mortality

In general, it has been confirmed that nosocomial infections are associated with mortality, however multiple factors, for example birth weight and underlying illness, make substantial contributions to mortality in the same population and care must be taken in attributing death directly to nosocomial infection (Goldmann 1981b, 1983). For example, infants in neonatal intensive care units are more likely to have nosocomial infections but they are also more likely to have lower birth weights and specific underlying conditions. In one study the crude risk of mortality with nosocomial infection was 2.46 when not stratified by weight (Hemming 1976) but 1.73 when stratified by weight (Kleinbaum 1982) (Rothman 1982). Thus the crude risk ratio of 2.46 is confounded by birth weight and represents the joint effect of low birth weight and

nosocomial infection in causing mortality. From this data it appears that almost half of the crude overall mortality was the result of low birth weight or its correlates rather than infection. (Freeman 1987).

In the study of PICU nosocomial infection performed by Brown (1987) 7 patients died out of a total of 42 infected patients (17%) compared with an overall mortality rate of 3.4% in the PICU during the study period. This study did not characterize the population under review by means of severity of underlying illness and it was unclear whether mortality in infected patients reflected causality or merely identified a more severely ill group of individuals.

In 1988, Craven et al carried out a study in adult ICU subjects investigating nosocomial infection and fatality. Thirty risk factors (which included major nosocomial infections - urine, blood, wound, pneumonia, CNS, peritonitis/intra-abdominal) were univariately associated with fatality. After stepwise logistic regression analysis was performed qv, only nine risk factors remained significantly associated with fatality and these included only one site of nosocomial infection namely nosocomial intra-abdominal infection. Overall, the relative risk of fatality was increased three fold in patients who acquired a nosocomial infection (Craven 1988).

There have been some attempts to associate fatality with

specific bacterial organisms. Miller et al (1987) studied nosocomial blood stream infections in adult ICU subjects and suggested that if underlying disease and other demographic variables (age, sex, race) were accounted for, infection with either Candida species or Pseudomonas aeruginosa was an independent predictor of death. In addition, Pseudomonas aeruginosa, Candida species, Enterococcus, Enterobacter, Klebsiella pneumoniae and Serratia marcescens were predictors of the clinical features associated with shock.

In paediatric patients, there have been no formal studies associating specific pathogens and fatality though there are isolated reports of death from both gram positive and gram negative organisms. Reported outbreaks of nosocomial viral disease eg., RSV, adenovirus, enterovirus have also included fatalities. (Krasinski 1985). There is a high mortality associated with respiratory syncytial virus (RSV) infection in children with congenital heart disease and increased pulmonary blood flow (McDonald 1982).

1.5.3 Nosocomial infection and morbidity

With regard to the morbidity of nosocomial infection; here, conversion of real world events into categorical data presents formidable difficulties partly because of the fundamental problem of confounders, and also because there is a dearth of meaningful, descriptive terminology with which to express morbidity. Morbidity outcomes for the

patient and his parents are necessarily sociological and behavioural rather than purely biological and may only be applicable in one institution and one patient population. Terms commonly employed include: 'loss of school days', 'days not up to the bathroom', 'days not up to the playroom', 'inability to keep up with peers in activities'. Clearly, none of these is applicable to the measurement of morbidity in the acute environment of the PICU though, after discharge, some of these terms may become more appropriate.

Specific morbidity outcomes using biological diagnoses are more likely to be robust when applied to other institutions but in the critically ill child it may be impossible to distinguish on biological grounds, between the sequelae of nosocomial infection and the effects of the underlying disease itself. The clinical illness which follows nosocomial infection may vary in severity. In some instances there is little or no alteration in the patient's condition and infection constitutes mere 'nuisance value' while in others nosocomial infection may cause a significant clinical deterioration and may contribute to death, albeit in a patient who has fatal underlying disease.

1.5.4 Nosocomial infection and increased patient care expenditure

Studies carried out in adult general hospital populations, have demonstrated a positive association between nosocomial infection and prolongation of hospital stay / increased cost of patient care. (Freeman 1979, 1984) (Haley 1980c, 1981) (Scheckler 1980). Estimates are produced by comparing the length of stay of a group of infected patients with the length of stay of an uninfected, control group who are matched by primary diagnosis and operation (matched cohort study). Freeman in Boston City Hospital demonstrated that patients with a single nosocomial infection remained in hospital on average 13 days longer than matched controls, and those with two such infections remained on average 35.4 days longer. This study referred to general ward patients only, and not to ICU patients (Freeman 1979). In a study of acquired pneumonia in adult ICU subjects, Craig (1984) demonstrated a threefold increase in length of stay in infected patients versus a group of uninfected control patients. The main difficulty with cohort studies lies in finding adequate numbers of matching control subjects. An alternative strategy is to estimate prolongation of stay and increased cost of patient care by means of subjective impressions of clinicians. In general, estimates based on epidemiologic comparisons among patient groups have been substantially greater than those based on subjective impressions of physicians. Green

(1982) has used the geometric mean of the ratio of length of hospitalization of infected patients to matched controls and suggested that this is more accurate than previously used methods involving the arithmetic mean. Estimates of prolongation of stay are greater in incidence studies than in prevalence studies.

To date, there have been no estimates of prolongation of stay due to nosocomial infection in PICU patients though there have been some crude costing studies of nosocomial infection outbreaks in general paediatric patients. In the 1970s an outbreak of nosocomial gastroenteritis was estimated to cost at least US$ 800 per infection. (Pinner 1982). Infections caused by a number of viruses may prolong periods of hospitalization (Mufson 1973) (Hall 1975). In 1977, in a study of diarrhoeal illness in general paediatric patients, medical costs were estimated to be US$ 836 per infection. (Ryder 1977).

1.6 DESIRABLE FEATURES OF A METHOD OF INFECTION SURVEILLANCE FOR ROUTINE USE IN THE PICU

I now propose to review the prominent features of an ideal system of nosocomial infection surveillance, which would be suitable for routine use in the PICU. The general history of nosocomial infection surveillance is summarized in Chapter 2.1 along with strategies of surveillance which are currently in use.

The ideal system of surveillance for nosocomial infection would be efficient and would put the onus of responsibility on the bedside staff who are in the best position to determine cause and intervene with assistance from the Hospital Infection Control service. The SENIC Project report (section 2.1.3) recommended that strategies of surveillance for routine use should identify those patients predicted to be at high risk of developing nosocomial infection and then target intensive surveillance towards them. In this way cost is contained and at the same time surveillance maintains its hospital-wide scope.

In the Hospital for Sick Children, Toronto, members of the Infection Control Service (E. Ford-Jones, C. Mindorff et al) have developed a system of infection surveillance which endeavours to satisfy these requirements. The system - the Infection Control Sentinel Sheet (ICSS) has been used satisfactorily throughout the hospital since January 1986. The sensitivity of the ICSS may be unstable varying with the type, incidence and severity of nosocomial infection and with the patient population. It requires evaluation in the PICU with comparison against a standard of: daily bedside patient examination, performed by a physician, plus daily review of in-patient charts.

CHAPTER 2

ISSUES OF METHODOLOGY

SUMMARY

As discussed in Chapter 1, formal studies of nosocomial infection which have been undertaken so far in the PICU, are somewhat diverse in their purpose and methodology and methodology is described more precisely in some studies than in others. Because of these variations, it is difficult to draw conclusions from the results of individual studies and comparisons of results between institutions are hampered. Future studies of nosocomial infection in the PICU should address those areas of methodology in which substantial diversity has been demonstrated namely:

surveillance of nosocomial infection (case finding)

criteria for nosocomial infection

severity of illness scoring

expression of nosocomial infection rates

In the following chapter, I shall discuss each of these issues.

2.1 SURVEILLANCE OF NOSOCOMIAL INFECTION (CASE FINDING)

2.1.1. Introduction

It has been observed that individual reports of summary data do not control for the intensity of surveillance for nosocomial infection and different institutions employ different strategies for surveillance. Clearly infection rates vary in direct proportion to the intensity of effort to detect infection. Therefore, hospitals (and PICUs) with more vigorous surveillance methods may look 'worse' than those with less intensive programmes. (Haley 1985a). The difficulty and cost of standardising data collection methods and maintaining their reliability over time may hamper efforts to measure rates of nosocomial infection and furthermore, may preclude comparisons between institutions.

Patients in hospitals are particularly prone to infection and this may threaten the success of their treatment and even their lives. Over ten years ago, in the United States, the SENIC study (2.1.3) confirmed that infection surveillance, control methods and an infection control team reduced infection rates in hospitals (Haley 1985a). Nosocomial infection surveillance in its entirety includes data collection, statistical analysis, dissemination of results and action. (Hughes 1987). According to Eickhoff (1969) the following benefits may accrue from an effective programme of surveillance for nosocomial infection:-

1. Identification of nosocomial pathogens commonly encountered.
2. Estimates of the endemic level of nosocomial infection in the hospital as a whole and in individual high risk areas or services.
3. Early warning system for epidemics regardless of the cause or location.
4. Specific investigation through a readily available mechanism and study group.
5. Continuing emphasis, at all levels of hospital staff, of the necessity for scrupulous observance of hygiene principles.
6. Strengthening links between hospital personnel and Infection Control staff.
7. Comparison of infection rates with other institutions.
8. Satisfaction of requirements for hospital accreditation.

The last twenty years has seen the emergence of formal programmes, in most countries, for the prevention of hospital acquired infection. In 1983 the American Academy of Pediatrics (AAP) published guidelines for Pediatric Intensive Care Units (Committee on Hospital Care and Pediatric Section of the Society of Critical Care Medicine 1983) and emphasised the importance of preventing nosocomial infections within them. The initiation of preventive intervention requires the early and complete detection of infection with, in due course, a reduction in

its transmission. Detection (or surveillance) may identify both epidemic and endemic disease.

2.1.2 Historical

The history of nosocomial infection surveillance in North America spans a thirty year period (Hughes 1987). In the United Kingdom there is some experience in paediatric patients from fifty years ago. (McKhann 1938) (Harries 1935); the pivotal role of the 'infection control sister' was reported in the early 1960s. (Gardner 1962) (Davis 1963) (Bradberr 1966).

The classic prevalence surveys of nosocmial infections, at all sites, were conducted at the Boston City Hospital in 1964 by Kislak and in 1967 by Barrett. At about the same time six hospitals of 176 - 507 beds undertook pilot surveillance projects with the Center for Disease Control (CDC). In 1974 the SENIC Project (see below) was initiated and its results were published in 1985. In 1976 the Joint Commission on the Accreditation of Hospitals (JCAH) specifically addressed infection control standards and established requirements for accreditation in US hospitals. Surveillance for nosocomial infection became a requirement for hospital accreditation in Canada in 1983 (Canadian Hospital Accreditation Group).

2.1.3 SENIC Project

In January 1974 the Center for Disease Control (CDC) initiated the SENIC Project (Study on the Efficacy of Nosocomial Infection Control) to determine whether infection surveillance and control programmes established in a random sample of US hospitals had a significant influence on the subsequent change in the hospitals' nosocomial infection rates over a five year period. (Haley 1980a). The project was designed to study the efficacy question separately for infections involving four different sites namely urinary tract, surgical wounds, blood streams and lower respiratory tract (both post operative pneumonias and pneumonias in medical patients).

The final report of the SENIC study made several noteworthy observations. (Haley 1985). Importantly the nosocomial infection rate increased by an average of 3% annually in those hospitals that did not establish infection surveillance and control programmes between 1970 and 1976. The critical components of an optimally effective nosocomial infection surveillance and control programme were shown to include a balance between surveillance and control efforts, the presence of one infection control practitioner for every 250 hospital beds, a trained hospital epidemiologist and the reporting of surgical wound infection rates to surgeons. At the four sites studied, surveillance was most important in the prevention of post

operative pneumonias and nosocomial urinary tract infections.

The SENIC study was not able to determine precisely which methods and schedules should be used in performing surveillance for nosocomial infection. At the time of data collection most centres were detecting infections in most areas of the hospital on a continuous daily basis using ward rounds, review of laboratory reports and similar clinical activities. Only a few centres were relying on periodic prevalence studies (limiting surveillance to specific wards or units) or other 'targeted' surveillance methods. It was suggested that 'targeted' surveillance - limiting surveillance to groups of patients predicted to be at high risk of nosocomial infection, would reduce the expense of surveillance while maintaining its continuous hospital wide scope. It was concluded however, that further studies were needed to confirm that 'targeted surveillance' was as effective as the 'traditional approach' evaluated in the SENIC project.

In Chaper 1 section 6, I reviewed the prominent features of a system of nosocomial infection surveillance which would comply with the recommendations of the SENIC Project report. It is suggested that a novel system of surveillance, currently in routine use in the Hospital for Sick Children, Toronto approaches this ideal. The system - the Infection Control Sentinel Sheet (ICSS) is applicable

hospital-wide; it 'flags' patients at risk of nosocomial infection and targets more intensive surveillance towards them. One of the aims of this study will be to evaluate this method of 'targeted surveillance' in the PICU comparing it with the 'traditonal' approach of daily bedside examination and chart review.

2.1.4 Infection Control in the United Kingdom

In the United Kingdom the need for an organization to investigate and control infection in hospitals has been recognized for many years and recommendations have been made in a number of official publications (Medical Research Council 1941, 1944) (Ministry of Health 1951, 1959) (Central Health Services Council 1959). These were concerned principally with the establishment of control of infection officers (CIOs) and control of infection committees (CICs). In 1962 the appointment of an infection control sister was recommended (Gardner 1962), and subsequently the concept of an infection control team became well established. (Lowbury 1975). Recent, poorly controlled outbreaks of infection - such as the food poisoning caused by Salmonella at Wakefield Hospital - have focused attention on the strategies currently used for curtailing hospital infection and it is suggested that pre-existing arrangements, despite their success in most British hospitals, may require enhancement. (DHSS 1986).

In 1988 the Joint Department of Health and Social Security and the Public Health Laboratory Service commissioned the Cooke report - Hospital Infection Control - Guidance on the Control of Infection in Hospitals. The British government now wants health authorities to draw on this report and ensure that they have clear management arrangements for controlling hospital infection. The Cooke report identifies the district general manager (advised by the district's hospital infection control committee) as the individual responsible for the arrangements for infection control and recognizes the crucial role played by the infection control doctor. A report of a survey of the Hospital Infection Society in 1986 showed that 98% of all health authorities in England and Wales have control of infection officers, four fifths of whom are consultant medical microbiologists. (Howard 1988). Clinical demand, however, may make it impossible for a single handed microbiologist to provide a 24 hour service, and there may be justification for implementing the recommendation of the Royal College of Pathologists for two microbiologists in large hospitals. Similarly a single infection control nurse may no longer be adequate for districts with greater than 750 beds. (The requirement in the United States is for one nurse for every 250 beds).

2.1.5 Surveillance Strategies

As a rule, one method of surveillance is used in all clinical areas throughout an institution and surveillance is either prospective or retrospective. Prospective study involves monitoring the patient while he is still hospitalized; retrospective study involves post discharge review of medical records by a variety of personnel. The SENIC study showed the sensitivities of prospective and retrospective techniques to be similar (0.76 and 0.74 respectively) (Haley 1980b); other studies have also reported favourably on retrospective review. (Wenzel 1976) (Gross 1980). In contrast Birnbaum (1981) and Blake (1980) found retrospective review less acceptable. It would appear that retrospective review can be highly effective in identifying nosocomial infection, but rigorous training and quality control are required.

A number of acceptable strategies for the surveillance of nosocomial infection have been described and these are now reviewed in association with an appraisal of their merits and limitations. Systems of surveillance are either patient based or laboratory based and are summarised below:-

SURVEILLANCE STRATEGIES

PATIENT BASED

1) Outcome assessment - count nosocomial infections
   CDC method
   Limited periodic surveillance
   Kardex review
   Periodic prevalence survey
2) Process assessment - review procedures and practices.

LABORATORY BASED

1) Identifying nosocomial infections
   Surveillance for infections of all types
   Bacteraemia surveillance
   Critical organism surveillance
2) Identifying outbreaks - threshold analysis
3) Surveillance of the environment

2.1.5.1. PATIENT BASED STRATEGIES

1) Outcome Assessment

CDC Method

The Centre for Disease Control (CDC) patient based surveillance system remains the standard against which all other systems are judged. (CDC 1972) (Haley 1986). The daily activities consist of reviewing microbiology

department records for positive cultures plus ward rounds, daily if possible, to review the records of patients who are isolated, febrile or receiving special treatments/antibiotics. In addition, visits with nurses and physicians, as well as random chart review, are helpful. Other sources of information include personnel health, and post-discharge surveillance of neonates and patients who have undergone surgery. Autopsy reports are also considered a source of information though one recent study suggests that their value is limited (Crossley 1983).

The CDC system has the following advantages:-

a) It provides a current, hospital wide, comprehensive review of nosocomial infections.

b) It provides data that are comparable to those reported by other institutions. (Lynch 1985).

c) The causative organisms and their antibiotic susceptibilities are defined.

d) The Infection Control Practitioner (ICP) has a high profile.

The major disadvantage of the system is that it is very labour intensive - 50% of ICP time.

Limited Periodic Surveillance

In 1973 Chelgren and LaForce described their adaptation of the CDC method. Full surveillance of the CDC type is

performed for one month quarterly with interim surveillance for bacteraemia only.

This system has the following advantages:-

a) Time spent for surveillance is reduced (50% of ICP time during period of CDC surveillance, reduced to 5% of ICP time during interim surveillance).
b) Data can be compared with national data and reports from other institutions using similar techniques.

The major disadvantage of this method is the potential for missing problems during the period of interim surveillance.

Kardex Review

This system, described in 1976 (Wenzel 1976a), uses the Nursing Kardex(R) which is a form summarizing the nursing care plan for each patient. The Infection Control Practitioner (ICP) reviews the Kardex for each patient searching for predefined clues suggestive of infection e.g. soaks, antibiotics; surgery; indwelling devices. The medical records are then reviewed for evidence of nosocomial infection. The system is less time consuming than the CDC method (16 hours compared to 60 hours of ICP time per week); it may detect up to 82% of infections, but it is dependent on centralised nursing care plans which all hospitals do not have. Wenzel and colleagues evaluated the system in critical care areas and found that it detected

48% of nosocomial pneumonias and 45% of bacteraemias. (Wenzel 1981) (Landry 1982).

Periodic Prevalence Survey

In this method point prevalence surveys are performed (Latham 1981) and from such data incidence figures are inferred. (Rhame 1981) (Freeman 1981b). The relationship between incidence and prevalence of infection is discussed in 2.4.3.

2) Process Assessment

Rather than measure the outcome of nosocomial infection, compliance with patient care and infection control practices may be measured. (Friedman 1984). Measurement of compliance alone, without assessing outcome, is adequate when the practice being examined is known to be effective in preventing nosocomial infections. When the effectiveness of the practice is unknown, measurement of compliance is unsatisfactory.

2.1.5.2. LABORATORY BASED STRATEGIES

Some recent work (Gross 1980) has indicated that laboratory surveillance may be efficient but there are potential problems namely:-

a) failure to detect infections for which no useful culture is obtained e.g. deep surgical wound infection, ventilator associated pneumonia, otitis media.

b) failure of the laboratory to provide certain diagnostic tests e.g. viral culture.

c) failure to standardise the application of diagnostic tests.

1) Identifying nosocomial infections

Surveillance for bacteraemia

This is an important element of a surveillance programme because the positive predictive value of a blood culture for infection is high. (Rose 1977) (Holzman 1977). The problem with site specific surveillance is that it will fail to identify the majority of infected patients who are infected at other sites.

Organism specific surveillance

In this system a list of organisms, which are of epidemiological importance to an institution, is compiled e.g. methicillin resistant Staph Aureus, Clostridium difficile, aminoglycoside resistant gram negative bacilli. Complete case review is undertaken whenever a laboratory test, culture or otherwise, indicates infection is likely.

(Laxson 1984). The system has limitations similar to those of site specific surveillance i.e. it will fail to identify patients infected with 'unlisted' organisms.

2) Identifying Outbreaks

Systematic approaches for using laboratory information for detection of outbreaks have been described. (Warner 1961) (McGuckin 1979) (Parkhurst 1985) (Birnbaum 1984) (Schifman 1985). Usually a threshold is developed to signal significant deviations and when this is exceeded an investigation is automatically triggered.

3) Surveillance of the Environment

The role of environmental surveillance in infecton control programmes was once a major issue, but is less so today. The appropriate nature, scope and use of this activity are further discussed by McGowan (1981) and in the Centers for Disease Control - Guidelines for Hospital Environmental Control (1981).

Different strategies of infection surveillance have different advantages e.g. speed of lab based system, completeness of bed side exam, and also different secondary gain e.g. nurse reporting may increase interest in infection control. The relative merits of the systems have not been systematically quantified and currently hospitals

are encouraged to be flexible and responsive to specific needs rather than adopt a static approach. (Abrutyn 1987).

2.1.5.3 Sensitivities of different strategies of Surveillance

The sensitivities of a number of surveillance methodologies relative to bedside examination and chart review are tested in Table 2.

Table 2 Sensitivity of methods of case-finding for nosocomial infection

Method	Reference	Sensitivity
physician self report forms	Eickhoff 1969	0.14 - 0.34
fever	Wenzel 1976(a)	0.47
antibiotic use	Wenzel 1976(a)	0.48
fever + antibiotic use	Wenzel 1976(a)	0.59
microbiology reports	Eickhoff 1969 Wenzel 1976(a) Thoburn 1968 Haley 1980(b)	0.33 - 0.65
selected chart review using 'Kardex' clues	Wenzel 1976(a)	0.85
total chart review	Wenzel 1976(a)	0.90
Boston City Hospital method (bedside exam)	Kislak 1964	1.00
prospective chart review	Haley 1980(b)	0.52 - 0.90
SENIC pilot retrospective chart review	Haley 1980(b)	0.66 - 0.80
standard (bedside exam)	Freeman 1981(a)	1.00**

(Adapted from Freeman 1981(a) and Thompson 1987).

** by definition, all other sensitivities are referable to this standard.

2.1.5.4 Published PICU Studies - Surveillance Strategies Used

In the published PICU surveys; several combinations of the available surveillance systems have been used. The study by Welliver (1984) was performed hospital-wide; surveillance consisted of:-

1) CDC system - infection control nurse (ICN) review of microbiology reports and inpatient charts.
2) Kardex review - also done by ICN.
3) review of patient record at time of hospital discharge - trained medical records department clerk.

In the study by Donowitz (1986b) surveillance methodology was described as 'Prospective surveillance, routinely performed by trained infection control practitioners'. More precise details of surveillance methodology were unavailable.

Brown et al (1987) obtained infection data from patient chart review, radiology reports and results of microbiology studies. Infection control personnel daily surveyed the critical care area.

The study by Milliken et al (1988) which was performed in this institution, (Hospital for Sick Children, Toronto) used the CDC method i.e. review of microbiology reports and

inpatient charts by infection control nurses. To date, no study has performed a 'gold standard' of surveillance comprising daily bedside examination of patients plus daily review of in-patient charts.

2.1.6 Application of Diagnostic Tests

Observed infection rates depend in part on the propensity of physicians to order diagnostic tests (Haley 1985b). The failure to apply diagnostic tests will understate the incidence of those infections for which a culture or other diagnostic intervention is required. These include blood, lung and urinary tract infections and, of particular interest in paediatric patients, viral infection of the respiratory or gastrointestinal tracts.

2.2 CRITERIA FOR NOSOCOMIAL INFECTION

The second area of methodology which merits discussion, is the criteria used for nosocomial infection. Broadly speaking, any definition of nosocomial infection is somewhat artificial. In most studies infections are considered to be nosocomially acquired if the first sampling from which micro-organisms are obtained is on or after the third hospital day. Likewise, PICU nosocomial infection would be that developing after 72 hours in the PICU. Clearly such a definition does not guarantee that offending pathogens are, in the strictest sense, of hospital (or PICU) origin.

Infection criteria are not necessarily rigorous definitions of disease but rather operational terms agreed upon by key hospital staff for hospital use, which may or may not include microbiologic aetiology. The Centers for Disease Control (CDC) has provided criteria for definition of infection, but it is recognized that some of these are outmoded and some are too brief to cover many clinical situations. (US DHEW Publ. 87-8314, 1975).

Clearly certain definitions are inadequate - for example 'pus at site' for wound infections, a term which excludes deep post operative wound infections. Nosocomial pneumonia is difficult to define (and, therefore, to diagnose), particularly in ventilated patients. A number of

definitions exist and none is entirely satisfactory. Any definition which includes 'sputum production' is inadequate since it excludes pneumonia in young children where sputum production is usually absent. In intubated patients it may be difficult clinically to distinguish between bacterial colonisation of the tracheobronchial tree and nosocomial pneumonia; pulmonary infiltrates often occur on a non-infectious basis.

Salata et al studied endotracheal aspirates from intubated adult ICU patients and suggested that serial examination of aspirates for elastin fibres in association with graded Gram stains could provide a means of early diagnosis of nosocomial pneumonia in these subjects (Salata 1987). On the other hand Golden et al studied the use of Gram stained smears and semi-quantitative cultures of endotracheal aspirates to diagnose pneumonia in intubated patients in a paediatric intensive care unit and demonstrated a poor correlation firstly between endotracheal aspirates and radiographic findings and secondly between the microbiological findings in aspirates and the results of blood cultures and postmortem examinations. They concluded that endotracheal aspirates were of questionable value in diagnosing the presence of pneumonia or its aetiology in intubated patients in the PICU (Golden 1987).

The diagnosis of bacterial pneumonia in PICU patients is primarily based on clinical and radiographic findings and

definitions of infection should reflect this fact. The most useful definition is probably "infiltrate on chest Xray, not present on admission, and not attributable to a non-infectious cause, with or without microbiological confirmation".

With regard to bacteraemia; the CDC definition considers bacteraemia secondary to a focal infection as 'secondary bacteraemia' while the primary focus is tallied with other, similar primary infections. This contrasts with the SENIC Project definition which considered bacteraemia secondary to a focal primary infection and bacteraemia without a recognized primary infection in the same category.

Definitions of viral infections may be "clinical" or may require recovery of the agent (Welliver 1984). In focussed studies such as those reporting infection following cardiovascular surgery more precise terms have been used (Edwards 1983).

2.2.1 Published PICU Studies - Criteria for Nosocomial Infection

Criteria for nosocomial infection have been more precise in some studies than in others. Donowitz (1986b) defined nosocomial infections in the text of the methodology however only four sites of infection were detailed - blood stream, pneumonia, urinary tract and post operative wound

Milliken (1988) supplied definitions of nosocomial infection as an appendix to his paper. Nine sites of infection were discussed and blood stream infections were sub-divided into primary and secondary types. Other studies have made reference to the CDC criteria with or without modifications (Brown 1987) (Welliver 1984).

2.3 SEVERITY OF ILLNESS SCORING IN PICU PATIENTS

The third area of methodology which merits discussion is severity of illness scoring. To date, published studies performed in the PICU, have analyzed nosocomial infections in terms of site, clinical specialty and use of therapeutic procedures or devices. The severity of the underlying illness has not been measured in paediatric patients although it is recognized as the single most important factor determining the risk of acquiring infection and its outcome.

2.3.1 Historical

McCabe and Jackson first attempted to define a patient population, using severity of illness, in 1962. These workers studied adult patients with disease which they designated as 'non-fatal', 'rapidly fatal' or 'ultimately fatal', and identified that the nature and severity of the underlying disease was the most important factor determining the outcome of bacteraemia. In this

prospective study, the admitting house officer assigned every new admission to one of three groups based on the severity of the patients's illness at that time. This information was recorded on a work sheet on the front of the patient's medical record. The infection rates in patients with rapidly fatal, ultimately fatal and non fatal disease were 27.2%, 13.1% and 2.8% respectively. The reliability and validity of this classification have not been determined and furthermore their terms are not applicable in an institution dealing with emergent survivors e.g. neonatal graduates.

Conventional methods for classifying patients with respect to utilisation of health care resources are based almost exclusively on diagnostic criteria and staging (Horn 1983) (Gonella 1984). The greatest problem with staging methodology is the fact that it examines each disease separately but does not link disease to look at the total impact on the patient. Hence only the principal identified condition is used in the measure of severity of illness and other secondary conditions, unrelated to the principal illness, are not captured. Two systems available for general application are Diagnosis Related Groups (DRGSs) and the Johns Hopkins severity of illness score; both have evolved primarily for costing purposes.

2.3.2 Diagnosis Related Groups (DRG)

The Diagnosis Related Group based system of classification was developed at Yale University (Fetter 1981) (Grimaldi 1981); it assumes that each DRG contains a clinically related group of patients with similar utilization of resources. There are 470 DRGs of which 51 (10.8%0 relate exclusively to paediatric disease entities. The disadvantages of this system are firstly that teaching hospitals have a higher proportion of complex patients who are not identified and secondly, it does not capture important differences in the severity of disease within a diagnostic group (Horn 1983, 1985a, 1986) (Flint 1986) (Lagoe 1986) (McMahon 1986) (Pasternak 1986) (Phibbs 1986).

2.3.3 Johns Hopkins Severity of Illness Score

This system was developed in response to the weaknesses of DRGs (Horn 1985b). It assigns to each patient, at or after discharge, a severity of illness score on a four level scale determined from the score for each of the 7 different dimensions as follows:-

1) stage of principal diagnosis at admission - greatest extent of organ involvement.
2) complication of diagnosis as a result of therapy or hospitalization.

3) interactions - pre-existing problems other than the principal diagnosis and its complications.

4) dependency - level of care required.

5) non-operating room procedure - procedures are assigned to one of four levels with 3 and 4 required for life support; the highest level of procedure, rather than the total number of procedures, determines the score.

6) rate of response to therapy - principal diagnosis, complications and interactions. This refers to acute illness only and does not reflect change in underlying disease for which no progress is expected.

7) residual symptoms at discharge.

To determine the score a rater scores each of the 7 dimensions at one of 4 levels; by examining the pattern of scores, an overall 4 point scale score is assigned. The 4 levels of severity are an ordinal scale from least severe (level 1) to most severe (level 4). A comparison of four different types of hospital with respect to total costs and lengths of stay shows that the academic teaching hospital does not have significantly higher charges than other hospitals when severity of illness and major operating room procedures are controlled for. The principal limitation of this method is that, so far, the computer branch system has been validated only for adult patients and not for paediatric patients.

2.3.4 Clinical Classification Scoring

Clinical classification scoring is a qualitative assessment of care requirements (Civetta 1973) (Cullen 1976). Class I patients need only routine hospital care and are not normally admitted to the ICU. Class II patients are physiologically stable and are admitted to the ICU only for monitoring or observation; Class III patients are physiologicaly stable but need ICU nursing care; Class IV patients are physiologically unstable, and need frequent assessments and interventions by ICU physicians and nurses. This system can be applied to the PICU patient but obviously other factors, apart from severity of illness, influence the selection of patients for PICU admission. These other factors include hospital policy, and the available facilties for post-anaesthesia recovery and high dependency nursing.

2.3.5 Therapeutic Intervention Scoring System (TISS)

Therapeutic and monitoring modalities can be assessed using the Therapeutic Intervention Scoring System (TISS score) which quantifies the amount of therapy instituted in each patient and can be used to define underlying illness severity (Cullen 1974). The system consists of 76 therapeutic and monitoring interventions; one to four points are assigned based on invasiveness and complexity of the intervention. This system has been applied to PICU

patients (Rothstein 1982). For paediatric use 'frequent infusion of blood products' (normally 5 units of blood) is modified to 'use of 20ml/kg of blood'. Otherwise the system is similar to that used in the adult ICU. Balloon counterpulsation and extracorporeal membrane oxygenation (ECMO) are not routinely available in the PICU.

The limitation of the TISS score is that it reflects the severity of illness in a heterogeneous population only if one assumes that the pathophysiology of organ dysfunction follows common paths requiring standard interventions; that all physicians intervene similarly and appropriately at each level of critical illness; and that all levels of intervention can be supplied if necessary.

By assessing therapeutic needs the CCS and TISS systems only indirectly reflect severity of illness and more direct methods of assessment, based on physiological principles, are preferable.

2.3.6 Acute Physiology and Chronic Health Evaluation (APACHE Score)

In 1981 Knaus et al developed the first physiology based classification system to quantify severity of illness in adult ICU patients - the Acute Physiology and Chronic Health Evaluation (APACHE) score (Knaus 1981). The prototype employed 34 variables though this number was

later reduced to 12 when APACHE II was developed (Knaus 1985). The variables reflect mostly the cardiovascular, respiratory, neurologic and metabolic systems; the value recorded is based on the most deranged reading during the first 24 hours that the patient is in the ICU. The degree of deviation from normal is defined as either high abnormal range or low abnormal range with a maximum of 4 points assigned to each variable. The sum of the scores for each variable provides the Acute Physiology Score (APS). Age and severe chronic health problems reflect diminished physiological reserve and have been incorporated into the system.

While the APACHE system was not primarily developed to be used for individual patient treatment decisions, APACHE II can provide the clinician with a systematic evaluation and an improved understanding of how an individual patient's severity of illness influences outcome (Knaus 1982, 1983). The principal limitation of this system is that variable ranges are not age adjusted hence, it is not applicable to infants or children.

2.3.7 Physiological Stability Index (PSI)

In 1984 Pollack et al developed and published a severity of illness scoring system for use in the Paediatric Intensive Care Unit - the Physiologic Stability Index (PSI) (Yeh 1984). The PSI characterises the patient's severity of

illness by quantifying the degree of derangement in 7 major physiologic systems independent of diagnosis. The ranges of some of the measured variables are appropriately adjusted for different ages. The system evolved from meetings of paediatric intensivists; most of the PSI impacts on the respiratory, cardiovascular, neurologic and metabolic systems. A total of 34 routinely or frequently measured variables from these seven systems was chosen. After assessing the degree of abnormality, each variable was assigned a score of 1, 3 or 5 which reflected the clinical importance of the derangement, but not necessarily the amount of deviation from the normal value. A score of 1 was assigned for a variable range that was not sufficient to mandate a change in therapy. A score of 3 indicated sufficient concern that it would lead most physicians to change therapy. A score of 5 indicated an immediate life threatening situation. Individual scores are added to obtain the final PSI score. The system has been validated for ages above and below 12 months. Unlike APACHE, the PSI does not have a chronic health assessment. (In fact Knaus found this feature to be superfluous when using APACHE to predict outcome in adult patients). The admission day PSI is least affected by therapeutic interventions and probably reflects severity of illness the best. The PSI severity of illness scoring system is detailed in Figure 1.

Figure 1 Physiologic Stability Index (PSI)

	1+	3+	5+
Infants			
Blood pressure	55-65	40-54	<40
systolic (torr)	130-160	>160	
Heart rate	75-90	50-74	>220
(beat/min)	160-180	181-220	<50
Children			
Blood pressure,	65-75	50-64	<50
systolic (torr)	150-200	>200	
Heart rate	60-80	40-59	>200
(beat/min)	150-170	171-200	<40
All Ages			
Blood pressure, diastolic (torr)	90-110	>110	
Cardiac index [1/(min.m^2)]	2.0-3.0	1.0-1.9	<1.0
$avDO_2$(vol%)	<3.0	>6.5	
	5.5-6.5		
CVP (torr)	<0, >15		
PCWP/LA (torr)	<5, 15-25	>25	
Infants			
Respiratory rate (breath/min)	50-60	61-90	>90
Children			
Respiratory rate (breath/min)	30-50	51-70	>70
All ages			
PaO_2 (torr)	50-60	40-49	<40
PaO_2/FiO_2	200-300	<200	
$PaCO_2$ (torr)	<30, 45-50	51-65	<65
All ages			
Glasgow Coma Score	8-11	5-7	<5
Intracranial pressure (torr)	15-20	21-40	>40
Seizures	focal	grand mal/status	
Pupils	equal-sluggish	unequal-dilated sluggish	fixed/ dilated

(continued/)

(continued)

Figure 1 Physiologic Stability Index (PSI)

	1+	3+	5+
All ages			
Hemoglobin (g/dl)	18.0-22.0	3.0-5.0	<3.0
	5.0-7.0	22.1-25.0	>25.0
WBC (cell/mm^3)	3-5,000	<3,000	
	20-40,000	>40,000	
platelets (cell/mm^3)	20-50,000	<20,000	
PT/PTT	>1.5 x control		
FSP (ug/ml)	>40		
All Ages			
BUN (mg/dl)	40-100	>100	
Creatinine (mg/dl)	2.0-10.0	>10.0	
Urine output (cc/kg/hour)	0.5-1.0	<0.5	
All ages			
AST/ALT (IU/l)	>100		
Amylase (U/l)	>500		
Total bilirubin (mg/dl)	>3.5		
Albumin (g/dl)	1.2-2.0	<1.2	
All ages			
Sodium (meq/l)	115-125,150-160	<115, >160	
Potassium (meq/l)	3.0-3.5	2.5-2.9	<2.5
Calcium (mg/dl)	7.0-8.0	5.0-6.9	<5.0
	12.0-15.0	>15.0	
Glucose (mg/dl)	40-60	20-39	<20
	250-400	>400	
Osmolality (mosm/l)	320-350	>350	
pH (U)	7.20-7.30	7.10-7.19	<7.10
	7.55-7.65	<7.65	
HCO_3	<16,>32		

It was postulated by Pollack and his co-workers that the different mortality rates observed within different PICUs were due to differences in patients' underlying severity of illness. This hypothesis was tested and confirmed in a multi-institutional study which used the PSI system to assess severity of illness, and which involved 9 PICUs across the United States. Results indicated that a six fold difference in mortality rates, observed initially between different institutions, disappeared when rates were adjusted for differences in severity of illness. (Pollack 1987). It was thereby confirmed that the most important predictor of mortality in the PICU was the severity of the underlying disease. Admission PSI scores of <10 generally correspond to low mortality risks (<5%); scores of 16-25 correspond with an observed mortality of between 30% and 40%; scores of >25 correspond with an observed mortality of >70%.

2.3.8 Paediatric Risk of Mortality (PRISM).

A simplified version of the PSI, the PRISM (Paediatric Risk of Mortality) score has subsequently been developed (Pollack 1988). The number of variables has been reduced to 23, and the measurement of all physiologic values is mandatory. This eliminates concerns about the assumption that if a variable is unmeasured then it is normal. Using the existing data base of 2642 patients from 9 PICUs, an estimation group and a validation group were formed.

Statistical techniques including univariate analysis and multivariate analysis were used to construct the PRISM score. The performance of PRISM was tested using goodness-of-fit tests and receiver operating characteristics (ROC) analysis. The PRISM score was demonstrated to perform equivalently to the organ weighted PSI system. The PRISM score for children is detailed in Figure 2 and that for infants is detailed in Figure 3.

Figure 2 PRISM Score Child

Variable	Value	Score
Systolic B.P.	150-200	2
(mmHg)	65-75	2
	>200	6
	50-64	6
	<50	7
Diastolic B.P.	>110	6
(mmHg)		
Heart rate	>150	4
(beats/min)	<80	4
Respiratory rate	51-90	1
(breaths/min)	>90	5
	apnoea	5
PaO_2/FiO_2[a]	200-300	2
	<200	3
$PaCO_2$[b]	51-65	1
(torr)	>65	5
Glasgow Coma Score[c]	<8	6
Pupils	unequal or dilated	4
	fixed and dilated	10
PT/PTT	1.5 x control	2
Potassium	3.0-3.5	1
(mmol/L)	6.5-7.5	1
	<3.0	5
	>7.5	5
Calcium	1.75-2.00	2
(mmol/L)	3.00-3.75	2
	<1.75	6
	>3.75	6
Glucose	2.0-3.3	4
(mmol/L)	13.8-22.0	4
	<2.0	8
	>22	8
HCO_3[d]	<16	3
(mmol/L)	>32	3

a Cannot be assessed in patients with intracardiac shunts or chronic respiratory insufficiency; requires arterial blood sampling.

b May be assessed with capillary blood gases.

c Assessed only if there is known or suspected CNS dysfunction; cannot be assessed in patients during iatrogenic sedation, paralysis, anaesthesia etc. Scores <8 correspond to coma or deep stupor.

d Use measured values.

Figure 3 PRISM Score Infant

Variable	Value	Score
Systolic B.P.	130-160	2
(mmHg)	55-65	2
	>160	6
	40-54	6
	<40	7
Diastolic B.P.	>110	6
(mmHg)		
Heart Rate	>160	4
(beats/min)	<90	4
Respiratory rate	61-90	1
(breaths/min)	>90	5
	apnoea	5
PaO_2/FiO_2[a]	200-300	2
	<200	3
$PaCO_2$[b]	51-65	1
(torr)	>65	5
Glasgow Coma Score[c]	<8	6
Pupils	unequal or dilated	4
	fixed and dilated	10
PT/PTT	1.5 x control	2
Bilirubin	age> 1 month; >60	6
(mmol/L)		
Potassium	3.0-3.5	1
(mmol/L)	6.5-7.5	1
	<3.0	5
	>7.5	5
Calcium	1.75-2.00	2
(mmol/L)	3.0-3.75	2
	<1.75	6
	>3.75	6
Glucose	2.0-3.3	4
(mmol/L)	13.8-22	4
	<2.0	8
	>22	8
HCO_3[d]	<16	3
(mmol/L)	>32	3

a Cannot be assessed in patients with intracardiac shunts or chronic respiratory insufficiency; requires arterial blood sampling.

b May be assessed with capillary blood gases.

c Assessed only if there is known or suspected CNS dysfunction, cannot be assessed in patients during iatrogenic sedation, paralysis, anaesthesia etc. Scores <8 correspond to coma or deep stupor.

d Use measured values.

2.3.9 Severity of Illness - Concepts and Measurements

Having reviewed the strategies available for quantifying severity of illness, I would like to briefly consider some of the associated fundamental concepts. This discussion is based on an article by Stein et al published recently in the Lancet (Stein 1987).

Severity of illness is not an absolute concept and, depending on whether severity is a predictor, a control or an outcome variable, different measures will be of interest. Even when a biological manifestation of a condition can be identified, severity cannot be quantified because the clinical manifestations are the product of interactions between biological determinants, genetic composition and environment. Hence, to grade severity, categories are employed similar to those used for assessment of socioeconomic status or intelligence. In essence, three categories of illness severity are recognized and commonly measured - physiological (or morphological) severity, functional severity and burden of illness.

2.3.9.1 Physiological Severity

Physiological status is assessed quantitatively from laboratory tests or anatomical reports. These measures reflect interactions of biological severity with

environmental factors including medical treatment. Overall physiological severity indicators are of little use in patients with rare conditions or multiple health disorders, or across a spectrum of different conditions. Many conditions lack markers and, where primary conditions are accompanied by other disorders, the combined effects are not necessarily additive. Furthermore, although a given marker may change as a result of several conditions, most markers do not apply across disease categories. Exceptions to this rule of condition specificity are the APACHE system (Knaus 1985) and the PSI/PRISM systems (Yeh 1984) (Pollack 1984, 1987c) though, in fact, some workers consider these systems to provide a measure of functional status rather than physiological severity.

2.3.9.2. Functional Severity

Functional severity is the impact of the disorder on an individual's ability to perform age-appropriate activities, irrespective of illness type, and under a broad range of circumstances. Functional severity reflects the effect of a condition on a final common pathway; namely the ability to conduct daily life. It is often assessed by items such as days missed from school or work, intellectual dysfunction due to disease, or the inability to play games or climb stairs.

2.3.9.3. Burden of Illness

Severity may also vary in terms of the impact of the disease or condition on the family or on society and this concept is the burden of illness. Any condition may be viewed as severe if it places a large burden on society in financial, emotional or social terms. Burden of illness measures, like functional severity measures, are applicable across diseases. The economic burden of illness underlies the DRG reimbursement system (see Section 2.3.2) and the Johns Hopkins scoring system (see Section 2.3.3).

2.3.9.4 Implications

A framework for defining illness severity may aid in clarifying assumptions underlying clinical and health care research. Three interacting categories may be distinguished. Most measures of physiological or morphological severity are disease specific and are affected by medical management and patient compliance. Functional severity indicates the effect of the disease on the person's ability to do things healthy peers do and is applicable where multiple conditions co-exist or across different diseases. Burden of illness includes the impact on the family and on society, and also applies across diseases.

2.4 EXPRESSION OF NOSOCOMIAL INFECTION RATES

2.4.1 Incidence of Infection

The occurrence of nosocomial infections is most often computed by dividing the number of infections acquired during a given month by the number of patients discharged (or admitted) during that month (Freeman 1981a). This parameter is called the infection rate, the incidence rate, or, less properly, the incidence. This derivation has the following associated problems:-

1) the duration of stay is ignored
2) the denominator excludes patients if they were not admitted and discharged within the same month
3) the 'rate' is really an incidence ratio
4) the 'rate' precludes inter/intra hospital comparisons
5) the 'rate' fails to recognize simultaneous infections in one individual

Although more complicated to calculate, a definition of the nosocomial infection rate as infections per 1,000 patient care days will correct for long hospital stays and avoid falsely high estimates of infection rates. This will allow comparisons of infection rates over time and across locations by separating the effect of long hospital stay from the effect of high daily risk.

In the SENIC Project the following measures were calculated. (Haley 1985a):-

The Infection Percentage - the percentage of admissions in which one or more infections occurred.

The Infection Ratio - the ratio (times 100) of the total number of nosocomial infections to total admissions.

The Incidence Density - the ratio (times 1,000) of the total number of nosocomial infections to the total number of days of hospitalization spent by all patients admitted to the hospital during a 12 month period.

The assumption is made that the number of admissions equals the number of discharges and the duration of stay is constant.

2.4.2 Prevalence of Infection

The prevalence rate is determined at a single point in time (Freeman 1980). The number of both active and cured nosocomial infections that are or have been present in patients hospitalized on a given day is divided by the number of patients present at the time of the survey. Both active and cured infections are included because of the difficulty in deciding the point at which an infection becomes cured. In practice, the 'single point in time' is

usually taken to be the interval (generally several hours) during which the survey team visits the ward. Since very few patients acquire a nosocomial infection during the first few hours of hospitalization, this comes very close to a true point of prevalence.

2.4.3 Relationship between Incidence and Prevalence

The following mathematical equation associates incidence (I) and prevalence (P).

$$I = P \times \frac{LA}{LN - INT}$$

I = incidence rate of nosocomial infection

P = prevalence rate of nosocomial infection

LA = mean length of hospital stay for all patients

LN = mean length of hospital stay for patients who have one or more nosocomial infections

INT = mean interval from admission to the first nosocomial infection in those patients who have had one or more nosocomial infections.

CHAPTER 3

ETHICAL CONSIDERATIONS

ETHICAL CONSIDERATIONS

3.1 BACKGROUND

It is recognized that an epidemiological study of this kind involves the accumulation and storage of large amounts of patient related data which, in turn, raises questions of an ethical nature particularly with regard to medical confidentiality.

Principles of bioethics have evolved from about the 16th century BC (Ad hoc Committee on Medical Ethics 1984). In this century; in 1948 the World Medical Organization adopted the Declaration of Geneva; the Nuremberg Code and the Declaration of Helsinki followed. The latter two deal more specifically with human experimentation.

Broadly speaking, ethical issues have been perceived in epidemiology for more than ten years and were first addressed by Susser et al in 1977 who dealt with problems regarding the choice of research questions, research design and the use of human subjects in research. In 1978, their dissertation entitled "Ethics in Epidemiology" was published in the Annals of the American Academy of Political and Social Science (Susser 1978).

At about the same time Gordis addressed questions of access to data, data privacy and the limitations imposed on

epidemiologic research through inaccessability to data sources. (Gordis 1977). For additional discussion regarding ethics in epidemiology the reader is referred to the excellent review article, published recently by Soskolne, entitled 'Epidemiology: questions of science, ethics, morality and law' (Soskolne 1989).

The concept of medical confidentiality is almost as old as medicine itself. The Hippocratic Oath, (or its modern counterpart the Declaration of Sydney), represents the roots which sustain the intra-professional code of conduct, and that is, in practice, the patient's main safeguard of what is generally considered to be his right. (Walters 1974, 1982). In Principles of Biomedical Ethics, Beauchamp and Childress argue that patient confidentiality and privacy are based on the fundamental principle of autonomy or respect for persons, though exceptions to confidentiality are sometimes necessary from a practical standpoint and are also morally defensible (Beauchamps 1983).

Problems have emerged over the past three decades concerning the use of confidential medical information in research, particularly when the investigator is not involved in the care or treatment of the individual concerned (Gordis 1980).

3.2 USE OF COMPUTER PROGRAMMES IN CLINICAL MEDICINE

With regard to medical confidentiality; clearly there is no necessary difference in content between conventional written records, and data in computer systems. The efficiency of automated systems may make violation of medical confidentiality easier, and, because of the amount of data on file, the damage to the patient may be proportionally greater. Computer systems and computers, therefore, involve a special degree of responsibility for those who control them (Miller 1985).

Over the last twenty years various countries have legislated on the question of access to, and protecton of, personal data held in computer banks. The State of Hessen, Federal Republic of Germany, was the first to do so in 1970 (International Commission of Jurists).

The British Government legislated in 1984 when Parliament passed the Data Protection Act. The protection of persons, about whom computerized information is stored, lies essentially in preventing the holding of inaccurate information or of concealing the fact that information is stored at all. Under the Act the subject of the data has the right to see that which pertains to him and to ensure its accuracy.

The Government of the United States of America enacted data protection legislation in the Privacy Act 1974 and in 1981 refinements were made concerning the data systems of the National Center for Health Statistics. In fact, by 1984, the privacy laws in the United States had been found to be an impediment to the conduct of epidemiological research, and a formal report was made on this problem by the US Environmental Protection Agency in 1984 (Task Force on Environmental Cancer and Heart and Lung Disease, 1984).

Recently Blake has reviewed issues of confidentiality associated with the use of computerized medical records. (Blake 1982). She implies that developments in the legal arena require hospitals and others in charge of such records to take special precautions against unauthorized disclosure of identifiable medical information. In Blake's opinion, specific guidelines should be used to avoid legal liability for breach of patient confidentiality however, restrictions should be carefully formulated and there must be a compromise between assuring patient confidentiality and providing necessary patient information to treating physicians.

The technology for protecting information stored on computers is not perfect (Gillard 1983) (Brannigan 1984) (Bruce 1984) (Covvey 1981). Several points of access in electronic information systems allow access to confidential information. The first is on-site personnel, both

authorized and unauthorized, who use terminal or dial-up lines in an 'authorized' manner to obtain and distribute information improperly. Also obtaining printed information that has been left unattended (e.g. in waste-paper baskets) is another on-site means of access to privileged information. Dial-in lines connected to the computer are accessible to anyone with modems and terminals. These lines might be tapped directly, or in extreme circumstances sensitive electronic receivers might even be used to remotely decipher the electromagnetic radiation (signals) generated by poorly shielded computer or communication equipment. Also, outsiders can 'break in' by trying various log-in names and passwords until one is found that works, or by obtaining passwords from authorized persons.

In Britain in 1973 the Medical Research Council formed a Standing Committee on the Use of Medical Information for Research. Since the Data Protection Act 1984 these guidelines have been updated, (Medical Research Council 1985). Some of the recommendations are now reviewed:-

1 Appropriate arrangements should be made and enforced for adequate physical security of establishments where confidential medical information is stored and used.

2 Special computing arrangements should be considered e.g. separation and replacement by code of the identifying data from the main body of the record or the use of computer 'scrambler' codes or 'passwords'.

3 Those responsible for collecting and storing personal medical data should review at intervals the desirability of destroying material when its retention is no longer required.

4 Data of a general statistical nature (i.e. in a form that prevents identification of individuals) may be made available to other research workers.

At all times during the course of this study these guidelines were adhered to.

Entirely as an aside, separate ethical concerns are raised by the existence of computer-based medical decision making and programmes capable of providing medical advice directly to the public. So far there have been no reported cases of injuries caused by computer soft-ware and it remains unclear whether liability would be tortious or would arise through breach of contract. Regardless, principles of negligence are well established (on both sides of the Atlantic) and these would apply should a case arise. For further discussion (United States law) the reader is referred to Brannigan (1981), Prince (1980) and Lanoue (1983).

3.3 INFORMED CONSENT

During the design of this study, the draft Revised Procedures on Research Involving Human Subjects, of the

Medical Research Council of Canada was reviewed. This study does not appear to raise any special concerns because of methodology, purpose or subject matter. There are no potential risks and no new material obtained apart from routine patient care. Informed consent, therefore, was not obtained from patients (or their parents/guardians) prior to their inclusion in the study.

CHAPTER 4

STUDY METHODOLOGY

Much of the methodology referred to in this volume is common to all the investigations which were undertaken and in order to avoid needless repetition the more important methods which were used will be collectively discussed in this section.

4.1 THE SETTING

The Hospital for Sick Children, Toronto, Canada is a 587 bedded, university affiliated, paediatric hospital which provides primary, secondary and tertiary care. The paediatric clinical specialties represented include general medicine, neonatology, cardiology, neurology, endocrinology, metabolic disease, immunology, general surgery, cardiovascular surgery, neurosurgery, orthopaedic surgery, maxillo-facial surgery, ENT and ophthalmology. The hospital provides a service for the management of trauma, burns and acute poisoning and is a regional centre for liver, kidney and bone marrow transplantation.

There is an 18 bedded PICU which admits approximately 1400 patients per annum with an average daily occupancy rate of 92% and an average daily census of 16.5 patients. (On occasion during the study, up to 4 beds in the Post Anaesthesia Recovery (PAR) area were used for patient care). Patients of all ages up to 18 years are admitted

with the exception of all premature neonates and neonates with non-surgical conditions who are admitted to the Neonatal Intensive Care Unit (NICU).

The following are the criteria for admission into the PICU:-

a) severe upper or lower respiratory tract distress demonstrated either solely on clinical grounds or in association with abnormal blood gas levels, increasing oxygen requirements, apnoea or altered level of consciousness.

b) cardiac insufficiency or dysrhythmia requiring close or precise monitoring.

c) suspected intracranial pathology requiring careful monitoring.

d) significant alterations of fluid, electrolyte, acid-base, temperature or coagulation status.

e) post operative state - All infants and children undergoing cardiac surgery are routinely admitted post operatively except neonates undergoing uncomplicated ligation of a patent ductus arteriosus. 40% of admissions are post operative cardiac surgery patients. The hospital has a post anaesthesia recovery area (PAR) which is staffed continuously 24

hours a day. With regard to all other post operative patients; as a general rule only those patients requiring ventilation in the immediate post operative period are admitted. All patients are admitted post operatively following liver and kidney transplantation.

f) another miscellaneous conditions e.g. patients admitted for investigation of pulmonary hypertension, patients on home ventilation programme admitted for sleep studies.

The PICU is situated on the second floor of the hospital with easy access to the operating theatres, recovery room and radiology department. The unit occupies a total area of 5,500 sq.ft., the patient care area accounts for 2,000 sq. ft., (approx. 100 sq. ft., per patient) with the remaining space devoted to staff offices, storage rooms, on-call rooms, staff washrooms and a conference room. During periods of maximum bed occupancy up to 4 'over spill' beds are available which are sited in the post anaesthesia recovery room (PAR) immediately adjacent to the PICU area.

The patient care spaces are divided into 3 four bedded rooms, one semi-private room with two beds, 3 isolation rooms with common ante room and one isolation room with its

own ante room. Each room has one sink. The unit is naturally ventilated.

The nursing staff provide patient care on a one to one basis; two clinical instructors and four assistant head nurses also participate in bed side care. The medical staff comprises four full time staff intensivists, ten medical residents and fellows, one anaesthesia fellow and a psychiatrist. There are no medical students or internes in the daily health care team. Other ancillary health care providers who have routine patient care include a physiotherapist, a respiratory technologist, a radiographer and a social worker. Consultations are provided in large numbers daily by fellows and staff in multiple specialties.

Visiting is restricted to immediate family members who are allowed to visit in groups of two. Children under 12 years of age are not allowed to visit unless with direct permission of the nurse in charge. The Hospital for Sick Children has an Infectious Diseases Department and this includes an Infection Control Physician and 4 Infection Control Nurses, one of whom has responsibility for the PICU. Surveillance results are returned to the Director and the Head Nurse within four weeks of the end of the month. There is a PICU Infection Control Committee which meets quarterly to review surveillance results, new procedures, policies and occupational health issues. Its members include the Infection Control Physician and the

Infection Control Nurse, a staff intensivist, a PICU Fellow, the Head Nurse, a clinical instructor of nursing and others by invitation.

An Infection Control Policy has been developed for physicians and surgeons and is detailed in Appendix 1. Specific nursing care procedures have been developed for surgical handwashing technique, management of intravascular lines, care of post operative cardiovascular patients, and prevention of nosocomial conjunctivitis. These are detailed in Appendices 2-5.

4.2 PATIENTS

During the period 1st July 1987 till 29th February 1988 a full time Research Fellow trained in critical care medicine and anaesthesia carried out this prospective study. A total of 685 patients, admitted consecutively, to the PICU were studied. Each patient was reviewed by the Research Fellow daily during the PICU stay and daily for 72 hours after PICU discharge. The following information was documented for each patient:-

a) Base-line state

b) The occurrence of nosocomial infection by site and pathogen

4.3 DEFINITION OF THE BASE LINE STATE OF THE POPULATION

The base line state of the PICU population was defined using the following.

a) PAEDIATRIC RISK OF MORTALITY (PRISM) SCORE

b) DEMOGRAPHIC DATA

4.3.1 PAEDIATRIC RISK OF MORTALITY (PRISM) SCORE

The literature on severity of illness scoring (including the PRISM score) is reviewed in Chapter 2 section 2.3 The PRISM score on admission to the PICU was derived by assessing the degree of abnormality of a list of variables and assigning a score of 1, 3 or 5 as previously described. The most abnormal value for each variable was used to calculate the score. On the day of admission at least 8 hours of data was required, otherwise the data was combined with the next complete collection interval. Scoring was done solely by myself using variables routinely documented by the nursing staff on the PICU flow sheets. The PRISM scoring system contains age adjusted variables and is applicable to infants or children. Figure 2 details the scoring system for children (age >1 year) and Figure 3 details the scoring system for infants (age <1 year).

4.3.2 DEMOGRAPHIC DATA

A specimen data collection sheet is detailed in Figure 4.

Figure 2 PRISM Score Child

Variable	Value	Score
Systolic B.P.	150-200	2
(mmHg)	65-75	2
	>200	6
	50-64	6
	<50	7
Diastolic B.P.	>110	6
(mmHg)		
Heart Rate	>150	4
(beats/min)	<80	4
Respiratory rate	51-90	1
(breaths/min)	>90	5
	apnoea	5
PaO_2/FiO_2[a]	200-300	2
	<200	3
$PaCO_2$[b]	51-65	1
(torr)	>65	5
Glasgow Coma Score[c]	<8	6
Pupils	unequal or dilated	4
	fixed and dilated	10
PT/PTT	1.5 x control	2
Potassium	3.0-3.5	1
(mmol/L)	6.5-7.5	1
	<3.0	5
	>7.5	5
Calcium	1.75-2.00	2
(mmol/L)	3.00-3.75	2
	<1.75	6
	>3.75	6
Glucose	2.0-3.3	4
(mmol/L)	13.8-22.0	4
	<2.0	8
	>22	8
HCO_3[d]	<16	3
(mmol/L)	>32	3

a Cannot be assessed in patients with intracardiac shunts or chronic respiratory insufficiency; requires arterial blood sampling.

b May be assessed with capillary blood gases.

c Assessed only if there is known or suspected CNS dysfunction; cannot be assessed in patients during iatrogenic sedation, paralysis, anaesthesia etc. Scores <8 correspond to coma or deep stupor.

d Use measured values.

Figure 3 PRISM Score Infant

Variable	Value	Score
Systolic B.P.	130-160	2
(mmHg)	55-65	2
	>160	6
	40-54	6
	<40	7
Diastolic B.P.	>110	6
(mmHg)		
Heart rate	>160	4
(beats/min)	<90	4
Respiratory rate	61-90	1
(breaths/min)	>90	5
	apnoea	5
PaO_2/FiO_2[a]	200-300	2
	<200	3
$PaCO_2$[b]	51-65	1
(torr)	>65	5
Glasgow Coma Score[c]	<8	6
Pupils	unequal or dilated	4
	fixed and dilated	10
PT/PTT	1.5 x control	2
Bilirubin	age> 1 month; >60	6
(mmol/L)		
Potassium	3.0-3.5	1
(mmol/L)	6.5-7.5	1
	<3.0	5
	>7.5	5
Calcium	1.75-2.00	2
(mmol/L)	3.0-3.75	2
	<1.75	6
	>3.75	6
Glucose	2.0-3.3	4
(mmol/L)	13.8-22	4
	<2.0	8
	>22	8
HCO_3[d]	<16	3
(mmol/L)	>32	3

a Cannot be assessed in patients with intracardiac shunts or chronic respiratory insufficiency; requires arterial blood sampling.

b May be assessed with capillary blood gases.

c Assessed only if there is known or suspected CNS dysfunction, cannot be assessed in patients during iatrogenic sedation, paralysis, anaesthesia etc. Scores <8 correspond to coma or deep stupor.

d Use measured values.

Figure 4 DATA COLLECTION SHEET I

Name		
Case No.		
Date of Birth		
Sex M/F		
Weight		
PICU admission date		
Admission PRISM score		
Admitting clinical specialty		
PICU discharge date		
PICU length of stay (days)		
Antibiotic on admission	prophylactic	Y/N
	empirical	Y/N
	therapeutic	Y/N
Steroid on admission	Y/N	
Immunosuppressant on admission	Y/N	
Infection on admission	community acquired	Y/N
	hospital acquired	Y/N
Date of Death		
Post mortem	Y/N	

The constituents of the demographic data collection sheet are described in more detail below.

age

hours, days, weeks, months, years.

clinical specialty/underlying disease

a) cardiovascular surgery (includes thoracic surgery performed by the department of cardiovascular surgery).

b) medical - general paediatric medicine
cardiology
neurology
metabolic disease
nephrology
endocrinology
acute poisoning
epiglottitis
laryngotracheobronchitis

c) trauma - includes burns and electrical shock

d) post-operative other:-
general surgery - includes liver transplant
urology - includes renal transplant
orthopaedic surgery
plastic surgery
ENT surgery
ophthalmology

e) haematology/oncology - malignant conditions
- bone marrow transplants

f) other - a group of miscellaneous unrelated conditions including:- near drowning,
congenital diaphragmatic hernia.

Length of Stay in PICU

The day of admission was defined as day one and each part of a day counted as one whole day e.g., admitted on Wednesday and discharged on Friday would be a PICU stay of 3 days.

Presence of Infection on Admission

Infection developing within 72 hours of PICU admission was deemed to be "incubating on admission" and infections present or incubating on admission were not considered to be PICU nosocomial infection unless they were clearly the result of a previous PICU admission.

Infection incubating on admission or already present on admission was considered to be either:-

1) hospital acquired - ward area of the Hospital for Sick Children or some other hospital.
2) community acquired

Examples of community acquired infection include:-

epiglottitis
laryngotracheobronchitis
meningitis
otitis media

For viral infection the following incubation periods were used (Valenti 1980):-

Upper Respiratory

no isolated virus	>3 days
influenza	>3 days
rhinovirus	>3 days
R.S.V.	>5 days
parainfluenza	>5 days
adenovirus	>7 days

Gastrointestinal

unknown aetiology	>3 days
Norwalk like	>2 days
salmonellosis	>2 days
rota virus	>3 days
campylobacter sp.	>3 days
shigellosis	1-7 days

When it was unclear if an infection was PICU acquired or hospital acquired/community acquired then the infection was <u>not</u> considered to be PICU acquired.

Pre-admission steroid therapy

This was documented. Topical and inhaled steroid therapy were not included.

Pre-admission immunosuppressant therapy

This was documented

Pre-admission antibiotic therapy

Antibiotics were further classified as:-

a) prophylactic

b) empirical (best bet, microbiologic sensitivities not available)

c) therapeutic (rational choice, microbiologic sensitivities available)

4.4 DOCUMENTATION OF NOSOCOMIAL INFECTION

Figure 5 DATA COLLECTION SHEET II

Date			
PICU day no			
blood			
CVP (sub clav)			
CVP (jug)			
CVP (fem)			
CVP (arm)			
CVP (umb)			
CVP tunnel			
CVP non tunnel			
ART (arm/foot)			
ART (fem)			
ART (umb)			
ART cut down			
ART per cut			
urine			
upper respiratory			
lower respiratory			
post-op wound			
chest drain			
peritoneal catheter			
other drain			
skin			
eye			
ICP cath/bolt			

Devices

The presence of each therapeutic device was noted along with its duration of use. When a device was removed it was recorded whether removal was because of infection or for some other reason e.g., no longer functional, no longer required.

Re-insertion of devices was documented. A coding system was used:-

P=device present;

X=device removed; (for reason other than infection)

S=device resited; (after removal for reason other than infection)

I=device infected;

R=device infected and removed;

A=device resited; (after removal because of infection)

arterial lines

Arterial lines were identified by anatomical site of insertion:-

peripheral artery - hand or foot

(radial, ulnar, dorsalis pedis, post, tibial)

arm - brachial artery

groin - femoral artery

umbilical artery

Arterial lines were also identified by technique of insertion:-

percutaneous

surgical cut down.

Central Venous Lines

Central venous Lines were identified by anatomical site of insertion:-

neck	-	jugular or subclavian vein,
arm	-	basilic or cephalic vein,
groin	-	femoral vein,
umbilical vein		

Central venous lines were also identified by technique of insertion:-

percutaneous,

surgical cut down,

surgical insertion with sub-cutaneous tunnelling

intracranial pressure monitoring device

bolt or catheter

chest or pericardial drain

peritoneal drain

includes peritoneal dialysis catheter

other cavity drain e.g., Jackson Pratt drain

4.5 SURVEILLANCE FOR NOSOCOMIAL INFECTION (case finding)

Definition of Bedside Observation

The Research Fellow undertook bedside observation a minimum of six days per week which comprised:-

selective clinical examination of patients,
review of PICU flow charts,
questioning of nursing staff,
review of medical and nursing notes,
review of microbiology reports,
review of other pertinent investigations e.g., tissue biopsy,
review of chest xrays - these are reported 5 days per week by one PICU dedicated radiologist,
review of drug Kardex,
in the event of death and autopsy - review of autopsy report and if possible attendance at the autopsy.

4.6 DEFINITIONS OF INFECTION

The following definitions of infection were used:-

Bacteraemia

positive culture of any organism, rule out contaminant (i.e., one isolate and patient recovered with no treatment).

1. Primary

unknown source

2. Vascular Line Related (arterial and central venous line)

Levels of evidence of infection in decreasing order of significance were:-

1) positive line blood culture + one or more positive peripheral blood cultures,
2) positive line tip + one or more positive peripheral blood cultures,
3) positive line tip + one or more positive line blood cultures,
4) positive line tip + positive culture from line exit site,
5) positive line blood culture + positive culture from exit site,
6) positive culture from exit site + positive peripheral blood culture,

7) compatible clinical situation with no other source + two positive blood cultures,

8) compatible clinical situation with no other source + one positive blood culture,

9) compatible clinical situation with no other source + positive culture from exit site,

10) compatible clinical situation with no other source + positive culture of line tip,

11) vascular line blood only,

12) CVL blood + arterial line blood only (no peripheral sample).

Respiratory

Organisms cultured from aspirates of endotracheal tubes or tracheostomies were not considered evidence of infection. In a very small number of patients aspirate from direct bronchoscopy or tissue from open lung biopsy were available for culture.

Upper Respiratory

Clinical diagnoses included:-

otitis media:- fever and red or bulging ear drum +/- middle ear effusion,

glossitis

stomatitis

tonsillitis

Clinical diagnosis by ward staff in collaboration with the infection control service for which microbiologic confirmation is not essential.

Lower Respiratory

The definition of infection used was:-

a) infiltrate - on chest xray,
not present on admission,
not attributable to a non infectious cause

b) plus or minus microbiological confirmation,

In difficult cases a consensus decision was made by the attending PICU physician and the staff radiologist.

Gastrointestinal

Two loose stools in 24 hours with or without identification of virus on electron microscopy / postive bacterial culture. Clinical picture must be compatible and other entities must be ruled out.

Necrotising colitis diagnosis requires clinical and xray features +/- positive C. Difficile blood titre.

Eye

1) Positive culture of recognized pathogen in association with:-

purulent conjunctival discharge

or,

oedema of the eyelid

or,

hyperaemia of the inferior palpebral conjunctiva,

2) Endophthalmitis / corneal opacification.

Skin

Most cutaneous sites were diagnosed by clinical criteria - pus in skin or subcutaneous tissue +/- positive culture of pathogen. This group included skin infection at the entry sites of devices e.g., drains, vascular lines.

NOTE If skin infection of a vascular line entry site was accompanied by other features of vascular line infection then this was documented as 'blood vascular line related' see section 3.6.1.2

Endocarditis

Endocarditis Surgical

early	<30 days since surgery
late	>30 days since surgery

Endocarditis Non-Surgical

No previous cardiovascular surgery.

Post operative Wound

1. Post operative wound (excluding sternal wound)

This required clinical evidence of infection i.e., surrounding erythema +/- purulent drainage at wound site +/- microbiological evidence.

2. Sternal Wound Infection

superficial early	infection limited to skin and soft tissue overlying the sternum +/- bacteraemia. <30 days since surgery.
deep (mediastinitis) early	infection extending to the sternum and/or mediastinal contents, +/- bacteraemia. <30 days since surgery.
superficial late	as above, >30 days since surgery.
deep (mediastinitis) late	as above, >30 days since surgery.

Urine

All samples were obtained via a urinary catheter either indwelling or intermittent or from supra pubic bladder aspiration. 'Clean catch' specimens were not used to diagnose urinary infection. Infection was diagnosed when there were >100,000 colonies per ml. urine of any organism.

Chest Drain

Positive culture of either fluid or drain tip after drain removal (under strict aseptic conditions).

Note: infection at the chest drain entry site was classified as skin infection.

Peritoneal Drain (including Dialysis Catheter)

As above, positive culture of peritoneal dialysis fluid or tip of catheter.

Cerebro-Spinal Fluid (CSF)

Primary

Positive CSF culture or latex agglutination - no previous neurosurgery.

Secondary

Positive CSF culture or latex agglutination - previous neurosurgery including insertion of intracranial pressure (ICP) monitoring device or an external ventricular drainage device (EVD).

4.7 EXPRESSION OF NOSOCOMIAL INFECTION RATES

The nosocomially infected patient ratio (NIPR) was calculated by obtaining the number of patients who acquired one or more infections and dividing by the number of patients admitted to the PICU x 100. The nosocomial infection ratio (NIR) was calculated by obtaining the total number of infections divided by the total number of patients admitted to the PICU x 100.

4.8 STATISTICAL ANALYSIS

Throughout the study several statistical methods were used as indicated. These include the two tailed Fisher exact test; chi-square analysis; and the Mantel-Haenszel procedure.

CHAPTER 5

NOSOCOMIAL INFECTION IN A PAEDIATRIC INTENSIVE CARE UNIT: INCIDENCE AND USE OF THE PRISM SCORE AS A PREDICTOR.

NOSOCOMIAL INFECTION IN A PAEDIATRIC INTENSIVE CARE UNIT: INCIDENCE AND USE OF THE PRISM SCORE AS A PREDICTOR.

SUMMARY

Between July 1987 and February 1988, all patients admitted to the Paediatric Intensive Care Unit (PICU) were classified using the PRISM score and followed, for the development of nosocomial infection, by a full time Research Fellow trained in intensive care medicine. Variables including clinical specialty, age, and PICU length of stay were identified.

During the study period 685 patients were admitted; 48 patients developed 100 nosocomial infections (7 infected patients per 100 patients admitted; 14.6 infections per 100 patients admitted). Patients with PRISM scores $\geq$10 on admission were significantly more likely to acquire infection than those with scores $<$10 (10.8% v, 3.4%, $p < 0.001$). This association held through age, clinical specialty and length of PICU stay. The sensitivity, specificity, positive and negative predictive values of a PRISM score $\geq$ 10 were 75%, 53%, 11% and 97% respectively.

As a percentage of total infections, bacteraemias accounted for 36% skin/eye/drain site infections for 22%, respiratory infections for 16%, wound infections for 15%, and urinary tract infections for 9%.

As a percentage of organisms causing infection, the most prevalent pathogens were coagulase negative staphylococci (CONS) (32%), Pseudomonas aeruginosa (23%), Candida sp. (20%) and S. aureus (9%).

A PRISM score ⩾10 on admission to the PICU characterizes a population within the PICU at increased risk of infection. However, 93% of patients did not develop infection and thus a negative predictive value of 97% yields little additional information.

5.1 INTRODUCTION

Nosocomial infection rates vary widely among different types of Intensive Care Unit, from 1% in cardiac surgical units to 25% or greater in medical, surgical and neonatal units. (Northey 1974) (Thorp 1979) (Chandrasekar 1986) (Hemming 1976) (Daschner 1982).

There are few data providing rates in the paediatric ICU (Brown 1987) (Donowitz 1982, 1986b) (Welliver 1984) (Milliken 1988) (Jarvis 1987, 1988) and rates in neonatal ICUs have sometimes been presented as PICU rates (Massanari 1986). Among published reports, the incidence of nosocomial infection has ranged from a low of 3.0% in a 3 bed unit (Donowitz 1982) to 24.1% (Jarvis 1988). A previous study has been undertaken in this PICU (Hospital for Sick Children, Toronto), based on twice-weekly chart review plus review of microbiology reports 5 days per week performed by two Infection Control nurses. Over a period of 30 months, 116 infections occurred in 1,388 patients who remained in the PICU for a minimum of 72 hours (6.1 infections per 100 admissions) (Milliken 1988).

A limitation of all the studies, performed to date, is the failure to adequately describe the baseline state of the population to enable comparison between institutions or within institutions over time. A severity of illness scoring system, the Physiologic Scoring Index (PSI) has

been validated as a predictor of mortality in the PICU (Yeh 1984) (Pollack 1987a, 1987b) and has recently been adapted to a shorter version - the PRISM score. (Pollack 1987c, 1988).

The aim of this study was to characterize the PICU population by PRISM score on admission as well as other traditional demographic data; to document the incidence of nosocomial infection by site and clinical pathogen in this group, and to report the use of the PRISM score as a predictor for the development of nosocomial infection.

5.2 METHODOLOGY

5.2.1 General

The study was performed using the general methodology described in Chapter 4. Patients were characterized by certain demographic data as well as PRISM score on admission and were reviewed daily for the development of nosocomial infection while in the PICU and for 3 days after discharge. Nosocomial infections were described by site and clinical pathogen using the criteria for infection, surveillance method, culture methods etc. already described.

5.2.2. Statistical Analysis

The nosocomial infection rate was calculated as the number of nosocomially infected patients per 100 patients admitted during the 8 month study period. Specific nosocomial infection rates were calculated for subgroups of patients based on the admission PRISM score, length of PICU stay, age and clinical specialty.

Chi-square analysis was used to compare the infection rates of patients with high and low PRISM scores. The Mantel-Haenszel procedure was used to compare infection rates in the two PRISM groups across the levels of a third grouping variable. Sensitivity, specificity, predictive values and power were calculated using standard methods.

5.3 RESULTS

During the eight month period, 685 patients were admitted to the PICU of whom 480 remained for 48 hours or more. 16 patients (2.3%) were admitted with nosocomial infections acquired in HSC or elsewhere (in another referring hospital) and 40 patients (5.8%) were admitted with a community acquired infection. While in the PICU, a total of 48 patients (7%) developed 100 nosocomial infections (15 infections per 100 patients admitted). 130 patients (19.0%) were receiving empiric or therapeutic antibiotic therapy on admission; 378 (55.2%) were receiving prophylactic antibiotic therapy on admission, reflecting the high proportion (69%) of trauma patients and post operative surgical patients (cardiac surgery and other surgery). 17 patients (2.5%) received steroid therapy prior to admission and 12 patients (1.8%) received immuno-suppressive therapy prior to admission.

The population is characterized by PRISM score in Table 3; there were equal proportions of patients with PRISM scores <10 and PRISM scores ≥ 10.

Table 4 shows the frequency of nosocomial infection by PRISM score; significantly more infections were acquired in the PICU by patients with PRISM score ≥ 10 (35/333) than by those with PRISM score <10 (12/352); (10.8% vs 3.4%; $p < 0.001$).

Table 3 Proportional frequency of PRISM scores

July 1987 - February 1988

PRISM score on admission	Number of patients	Proportional frequency %
0 - 4	130	18.9
5 - 9	222	32.3
10 - 14	197	28.8
15 - 19	71	10.3
20 - 24	35	5.4
25 - 29	14	2.0
>30	16	2.3
TOTAL	685	100.0

Table 4 Frequency of nosocomial infection with PRISM score

Number of infections	Total no. patients	PRISM <10	PRISM ≥10
1	26	8	18
2	11	3	8
3	3	0	3
4	1	1	0
5	5	0	5
6	2	0	2
TOTAL	48	12	36

Table 5 shows the infection rates by PRISM score and length of stay in the PICU. PRISM score was significantly associated with length of stay ($p < 0.001$) accounting for much of the relationship of PRISM with infection rate. However, the predictive relationship of PRISM score and infection is apparent in longer PICU stays. For the Mantel-Haenszel procedure, length of stay categories >16 days were combined because of small numbers. The Mantel-Haenszel summary chi-square was not significant ($p = 0.10$) across all 4 length of stay groups, but was significant when only those with length of stay 7 days or more were analyzed ($p < 0.02$).

The relationship between PRISM score ≥ 10 and increased risk of nosocomial infection is demonstrable across age ranges (Table 6). The increased nosocomial infection rate with PRISM score ≥ 10 was observed throughout all clinical specialties (Table 7).

Table 5 Relationship of PRISM score and length of stay in PICU to nosocomial infection rate

PICU stay	Total		PRISM <10			PRISM ≥10		
(days)	n	% inf	n	no.inf	% inf	n	no.inf	% inf
<7	551	2.2	308	6	2.0	243	6	2.5
7 - 15	106	14.2	37	4	10.8	69	11	15.9
16 - 24	18	61.1	6	1	16.7	12	10	83.3
25 - 35	3	100.0	0	0	-	3	3	100.0
>35	7	100.0	1	1	100.0	6	6	100.0
TOTAL	685	7.0	352	12	3.4	333	36	10.8

n = number of patients

% inf = percentage of n who were infected

no.inf = number of patients within each PRISM group who were infected.

Table 6 Relationship of PRISM score and age to nosocomial infection rate

Patient	Total		PRISM <10			PRISM ≥10		
age	n	% inf	n	no.inf	% inf	n	no.inf	% inf
<30 days	62	11.3	13	1	7.7	49	6	12.2
31-180 days	88	11.4	38	0	0	50	10	20.0
6 mo-2 yr	122	7.4	63	3	4.8	59	5	8.5
2-10 yr	273	6.2	143	6	4.2	130	10	7.7
>10 yr	140	3.6	95	2	2.1	45	5	11.1
TOTAL	685	7.0	352	12	3.4	333	36	10.8

n = number of patients

% inf = percentage of n who were infected

no.inf = number of patients within each PRISM group who were infected.

Table 7 Relationship of PRISM score and clinical specialty to nosocomial infection rate

Clinical speciality	Total n	Total % inf	PRISM <10 n	PRISM <10 no.inf	PRISM <10 % inf	PRISM ≥10 n	PRISM ≥10 no.inf	PRISM ≥10 % inf
trauma	55	3.7	28	0	0	27	2	7.4
postop cardiac	314	9.4	138	9	6.5	176	21	11.9
postop other	106	2.8	66	0	0	40	3	7.5
oncology	10	10.0	5	0	0	5	1	20.0
medical	169	6.5	99	3	3.0	70	8	11.4
other	31	3.2	16	1	6.2	15	0	0
TOTAL	685	7.0	352	13	3.6	333	35	10.5

n = number of patients

% inf = percentage of n who were infected

no.inf = number of patients within each PRISM group who were infected

Multiple Infections

Two patients had 6 infections, 5 patients had 5 infections, 1 patient had 4 infections, 3 patients had 3 infections, 11 patients had 2 infections and 26 patients had one infection each. Of the 36 infected patients with PRISM scores ≥ 10, 18 (50%) had more than one infection compared to 4 (33%) of 12 infected patients with PRISM score <10 ($p > 0.5$).

Deaths

The overall mortality rate in the unit was 8.8% (60/685) with deaths in 8.5% of patients without nosocomial infection (54/637) and deaths in 12.5% of patients with nosocomial infection (6/48) ($p > 0.5$). This suggests that overall nosocomial infection rate does not increase mortality, although the power to detect a difference is low. Of those with PRISM scores <10, 11 (3%) died, of those with PRISM scores ≥ 10, 58 (17%) died ($p < 0.001$). Thus PRISM ≥ 10 predicts both mortality and nosocomial infection, but infection does appear to be directly related to infection.

Site of Infection

The relative frequency of nosocomial infection by site and PRISM score is listed in Table 8. It appears that the nosocomial infection rate from bacteraemia (all types) was higher in PRISM scores ≥ 10 but it is suspected that high score patients had more vascular lines and therefore were at greater risk of bacteraemia.

Table 8 Relative frequency of nosocomial infections by site and by PRISM score

Site	Total		PRISM <10		PRISM≥10	
	No Inf	NIR	No Inf	NIR	No Inf	Nir
Blood	12	1.8	5	1.4	7	2.1
CV Line	12	1.8	2	0.6	10	3.0
Art line	12	1.8	3	0.8	9	2.7
Resp.upper	6	0.9	3	0.8	3	0.9
Resp.lower	10	1.5	3	0.8	7	2.1
Postop wound	15	2.2	2	0.6	13	3.9
Urine	9	1.3	0	0.0	9	2.7
Skin	7	1.0	2	0.6	5	1.5
Chest drain	5	0.7	1	0.3	4	1.2
Peritoneal drain	4	0.6	0	0.0	4	1.2
Eye	5	0.7	2	0.6	3	0.9
SBE	1	0.1	0	0.0	1	0.3
T tube	1	0.1	1	0.3	0	0.0
Gastrointest.	1	0.1	0	0.0	1	0.3
TOTAL	100	14.6	24	6.8	76	22.8

No Inf = number of infections

NIR = Infections/100 admissions = Nosocomial Infection Rate

Patients with low PRISM scores were at risk from bacteraemias and respiratory infections while those with high PRISM scores had higher rates at virtually all sites including post operative wound infections. Bacteraemias and other line related infections accounted for 36% of infections; respiratory wound and skin/chest/peritoneal drain for approximately 15% each; urine 9%; eye 5% and other 3%. Seventy six of these 100 infections were in patients with PRISM $\geqslant$10 and this proportion was consistent across sites.

The relative frequency of organisms causing nosocomial infection is detailed in Table 9. Gram positive, gram negative bacteria and fungi accounted for 42%, 35% and 19% of infections respectively.

Table 9 Relative frequency of organisms causing nosocomial infection

Organism	No. Infections	Proportional % of all organisms
Bacteria		
Gram positive		
Coagulase negative Staph	29	29.6
S aureus	8	8.2
Group D strep	4	4.1
Gram negative		
Pseudomonas aeruginosa	21	21.4
Escherichia coli	1	1.0
Proteus mirabilis	1	1.0
Enterobacter cloacae	5	5.1
Enterobacter aerogenes	6	6.1
Fungus		
Candida sp.	19	19.4
Virus	0	0
other organisms		
TOTAL	100	

Experience with intravascular lines

Vascular line related infections were analyzed in terms of: the anatomical site of line placement, the method of line placement (surgical v percutaneous), the level of evidence for infection, the organisms causing infection and the length of time the line was in situ prior to infection. Levels of evidence for infection are detailed in Chapter 4, section 6; Criteria for Infection, vascular line related.

Central venous lines

In total 300 central venous lines were placed; infection occurred in 12 lines (4%). Lines were surgically placed (using a subcutaneous tunnel) in 21 cases (1 infection; 5%), otherwise, in 279 cases, lines were placed percutaneously (11 infections 3.9%). No infections occurred in 2 umbilical lines. Infections occurred in 1 of 21 tunnelled neck lines (5%), in 8 of 227 non tunnelled neck lines (3.5%), in 2 of 16 arm lines (12.5%) and in 1 of 34 femoral lines (2.9%). Table 10 details infected central venous lines.

Arterial lines

In total 494 arterial lines were placed; infection occurred in 12 lines (2.4%). Lines were surgically placed, using a cut down in 68 cases (2 infections, 2.9%).

Otherwise lines were placed percutaneously (426 cases 10 infections, 2.3%). No infection occurred in 5 umbilical lines or in 1 arm (brachial) line. Two infections occurred in 45 femoral lines (4.4%) and 10 infections occurred in 443 lines placed peripherally, in either the hand or the foot (2.25%). Table 12 details infected arterial lines.

Extended use of Lines

25% of arterial lines and 30% of percutaneous central lines are in situ >5 days. Arterial lines in situ >5 days are more likely to be infected (3/300 vs 9/119 or 1.0% vs 8.3%). Similarly, percutaneous CVLs in situ >5 days are more likely to be infected (9/75 vs 3/225 or 12% vs 1.3%).

Concurrent Infected lines

In 3 of 12 situations in which either arterial or central line cultures were positive, both arterial and central lines were culture positive.

Table 10 Central venous line related nosocomial infections

site	n	no.inf	% inf	organism	level of evidence*	line day of inf**
tunnel neck	21	1	5.0	PA	1	7
arm	16	2	12.5	diptheroids	8	4
				haem strept	10	13
non tunnel neck	227	8	3.0	dipth/CONS	1/5	12/35
				candida alb	1	11
				SA	2	3
				PA/E cloac	9	11
				candida alb	3	8
				PA/CONS	9/2	9
				candida para	9	8
				haem strept	10	4
femoral	34	1	2.9	ent strept/ candida alb	9	5
umbilical	2	0	-			
TOTAL	300	12	4.0			

* level of evidence of infection see Section 4.6 - definitions of infection, vascular line related infections

** line day of inf = day when line was first infected (day of line placement = day 1)

candida alb = candida albicans
candida para = candida parapsilopsis
P A = pseudomonas aeruginosa
S A = staphylococcus aureus
CONS = coagulase negative staphylococci
haem strept = haemolytic streptococci
ent strept = enteric streptococci
dipth = diptheroids

Table 11 Arterial line related nosocomial infections

site	n	no.inf	% inf	organism	level of evidence*	line day of inf**
femoral	45	2	4.8	CONS/PP	1	11
				CONS	11	2
periph	443	10	2.3	SA	1	4
				CONS	11	11
				CONS	1	9
				CONS	1	18
				CONS	11	1
				CONS	11	4
				CONS	11	10
				CONS	11	13
				CONS	11	13
				cand alb	11	11
umbil	5	0	-			
arm	1	0	-			
TOTAL	494	12	2.4			

* level of evidence of infection - see Section 4.6 - definitions of infection, vascular line related infections

** line day of inf = day when line was first infected (day of line placement = day 1)

P P = pseudomonas putida
S A = staphylococcus aureus
CONS = coagulase negative staphylococcus
cand alb = candida albicans

5.4 DISCUSSION

These data further define the epidemiology of nosocomial infections in the PICU by describing more precisely the baseline state of the study population. They lend additional support to the validity of the PRISM scoring system as a predictor of nosocomial infection as well as death. While the inter-relatedness of PRISM score and length of stay complicates interpretation of the study, it should be noted that the PRISM score identifies high risk patients on admission, rather than later in the stay. It is not clear whether risk of infection is a cause or effect of the high PRISM score. Preventive interventions, e.g., gown and gloves, might be of use in this specific high risk group. Possible intervention strategies, which may be applied to high risk patients, are discussed further in Chapter 9. Use of the PRISM score should be encouraged to characterize PICU patients and their risk of infection for comparative purposes. An alternative scoring system might be the Therapeutic Intervention Scoring System (TISS) which determines how much actual medical intervention is needed for each patient (see Chapter 2 section 3.5) although, it does not offer the additional benefits, provided by the PRISM system, unrelated to infectious diseases (Pollack 1988).

The sensitivity and specificity of a PRISM score $\geq$10 were 75% and 53% respectively. Paediatric patients with PRISM

scores ≥10 on admission to the PICU have a significantly greater risk of nosocomial infection despite differences in age and length of stay. The positive and negative predictive values of the PRISM score were 11% and 97%; thus those patients with a PRISM score <10 were unlikely to become infected. If the PRISM score were to be used as a "test" for whether or not a patient would later develop nosocomial infection, this report suggests it would have a sensitivity of 75%; that is, 75% of those with infection would be in the group with high PRISM scores. Unfortunately, the positive predictive value would be only 11%; that is, only 11% of those identified by their high admission PRISM score would later develop infection. The specificity of this test might be expected to be 53%; that is, of patients who do not become infected 53% would be found in the low PRISM group. The negative predictive value, 97%, means that the test is correct 97% of the time when it predicts that a patient will not become infected on the basis of a low PRISM score. It should be noted that in the study group overall, 93% of patients did not become infected, so guessing that nobody would become infected, would have a negative predictive value of 93%. Nevertheless, the admission PRISM score does characterize patients at higher risk of infection.

Reports of nosocomial infection in PICU patients have varied widely. (Welliver 1984) (Donowitz 1986b) (Brown 1987) (Milliken 1988) (Jarvis 1988). Previously measured

variables which may contribute to this are: differing size of the units; differing patient populations as measured by the percentage of patients admitted with nosocomial infection and the percentage of patients admitted with nosocomial infections acquired elsewhere in the hospital; differing proportions of patients in terms of clinical specialty, and differing mortality rates.

Definitions of nosocomial infection have been fairly consistent. Previously unmeasured variables include the intensity of surveillance, the application of diagnostic tests, baseline state of the population or underlying illnesses, as well as environmental and behavioural features such as education about, and compliance with, infection control policies for all full time and rotating staff.

In a previous study, performed in 1988 in this PICU (HSC, Toronto), Milliken documented differences among patients' risk of infection by age and by length of stay prior to the onset of the first nosocomial infection (Milliken 1988). Patients in the first two years of life, particularly those aged 7 to 30 days, have the highest rates of infection. Onset of infection was more common after the first week in the PICU with infections acquired by 11% of patients staying 14-20 days; 27% of patients staying 21-27 days; 48% of patients staying 28-34 days, and 52% of patients staying more than 35 days. The present study further

refines this finding by adjusting for PRISM score (Tables 5 and 6). Whether the global increase in infection since the 1983-85 report is due to improved intensity of surveillance (i.e., daily bedside review by dedicated Research Fellow/intensivist vs twice weekly chart review, lab reports) or other unmeasured factors is unclear. It is suspected that the current patient population is substantially sicker as new operative procedures, (particularly cardiac) requiring post operative PICU care are introduced and the use of indwelling intravascular lines is increased.

There are few data with which to compare the results of the present study. The work does confirm Milliken's earlier finding that viral disease is occurring at a far lower incidence in the PICU than in other parts of the Hospital for Sick Children where, for example, 8 to 10% of infants and young children acquire viral diarrhoea. (Ford-Jones in press). Unmeasured differences, which might explain this, are: less exposure to staff through one to one nursing ratios; fewer staff caring for infected and uninfected children; less visitors including siblings; personalized equipment and absence of child to child contact. Furthermore, patient hand/mouth contact is not possible.

Published data on pathogens are similarly sparse. This study demonstrates that gram positive pathogens are slightly more common than gram negative (42% vs 35%) and

viral pathogens are extremely uncommon. Of concern, is the increasing proportional frequency of fungal pathogens to 20% of the total; this reflects published experiences that fungal nosocomial infections are on the increase. Vascular line related infections have been analyzed in terms of site and method of placement. In the PICU, culturing of indwelling vascular lines presents problems, for example: inotropic agents being administered via central venous lines cannot be stopped for the duration of a culture without risk to the patient; meticulous culturing of multilumen catheters, with appropriate labelling of the ports may not be carried out.

It is routinely taught that to accurately diagnose catheter related bacteraemia, (as opposed to catheter colonization alone), simultaneous sampling of blood from a peripheral vein and from the vascular line should be performed. However, evidence for this presumption is somewhat scarce. Two studies (Tonneson 1976) (Felices 1979) refute the dictum and Holzman (1981) concludes that if the injection port of the catheter is properly cleaned with an agent containing iodine-povidone, valid cultures may be obtained via this route. Ideally, the completeness of culturing during a possible septic event should be recorded.

2.4% of arterial lines were infected; risk of infection increased with duration of catheter use but did not seem to be increased either by surgical cut down (cut down 2.9%

infected vs percutaneous 2.3% infected) or by insertion of lines in the groin. This compares with the results of a study of 130 arterial catheters by Band et al (1979) who reported a 4% incidence of line related sepsis and an increased risk of infection in association with both increasing duration of catheterization and placement of the catheter by means of surgical cut down. Adams (1980) reported catheter related sepsis in only 0.6% of radial artery catheters in new born infants, but mean duration of catheter placement was 48 hours or less. In this study, there was a preponderance of infection with coagulase negative staphylococci (83% cases); one line had a simultaneous infection with pseudomonas putida, an organism which is usually assumed to be a contaminant.

With regard to central venous lines; 4% of lines became infected which is in accordance with the observations of Maki (1973). Risk of infection increased with duration of catheter use and siting central venous lines in the ante cubital fossa but there was no apparent increase associated with the siting in the groin. It should be noted that numbers in the ante cubital fossa and groin groups were very small and conclusions should be guarded. CVL infections were caused by a wider range of organisms, though most were skin flora organisms (CONS, diptheroids). It has been observed previously that intravascular lines commonly are colonized by organisms of the skin flora (Maki 1973) (Crossley 1972) (Peter 1972) (Collins 1968) (Fuchs

1971). In the present study, candida species accounted for infection in 4 cases (33%). Maki (1973) reported infected central venous lines in 27% of patients with candida and other fungi responsible for more than 50% of these episodes.

CHAPTER 6

EARLY NOSOCOMIAL INFECTION IN PAEDIATRIC CARDIAC SURGERY PATIENTS

EARLY NOSOCOMIAL INFECTION IN PAEDIATRIC CARDIAC SURGERY PATIENTS

Focus on Operative Procedure and the Intensive Care Unit

SUMMARY

All patients who underwent cardiac surgery and were admitted to the Paediatric Intensive Care Unit (PICU) between July 1st 1987 and February 29th 1988 were reviewed:

1) for nosocomial infection at all sites - daily and for 72 hours after discharge from the PICU
2) for wound infection - for 2 months after surgery.

Patients were characterized by surgical procedure and PRISM score on admission to the PICU.

During the study period 310 patients were admitted. 40 patients (nosocomially infected patient ratio (NIPR) = 12.9%) developed 78 infections (nosocomial infection ratio (NIR) = 25.2), of which 28% were wound infections occurring within two months of surgery (n = 22). Early wound infection followed 8.0% of closed (non cardio-pulmonary bypass (non CPB)) cases and 6.7% of open (cardio-pulmonary bypass (CPB)) cases.

Wound infection was more likely if the sternum was open post operatively, while in the PICU (27.6% open sternum v 5.0% closed sternum p = 0.00028); if the PRISM score on

admission was ⩾10 (10.7% ⩾10 v 2.3% <10; p = 0.00344), and following specific surgical procedures.

The causative agents in wound infections in closed (non CPB) cases were Staphylococcus aureus (70%) and coagulase negative staphylococci (CONS) (30%) while in open (CPB) cases they were CONS (33%), P. aeruginosa (27%), Candida sp. (27%) and Staph aureus (20%).

Non-wound infections accounted for 72% of infections (n=56). The number of bacteraemias and other central venous line and arterial line related infections approximated wound infections in incidence at 6.8 infections per 100 patients.

6.1 INTRODUCTION

Wound infections occurring in paediatric cardiac surgery patients have been reported (Edwards 1983) (Culliford 1976), however infections have not been stratified previously either by operative procedure or by the status of the patient at the time of surgery. Furthermore, despite the introduction of complex intravascular monitoring devices, the incidence of non wound infections in paediatric cardiac surgery patients has not been formally documented. This study reports:-

1) nosocomial infections at all sites occurring in a population of paediatric cardiac surgery patients in the PICU.

2) early wound infections occurring within the first two months of surgery in the same group of patients.

6.2 METHODOLOGY

6.2.1 General

The study was performed in the setting, using the common methodology as described in Chapter 4.

6.2.2 Definition of population by surgical procedure

In addition to definition of the population by PRISM and demographic data, all patients were identified by type of surgical procedure (see Appendix 5 for procedures) and whether or not the sternum remained open in the post operative period. Patients where the sternum remained open post operatively were further divided into those where the sternum was electively left open at the time of surgery (delayed sternal closure) and those where the sternum was closed at the end of the surgical procedure and then subsequently required re-opening as an emergency procedure in the PICU. In this population, delayed sternal closure is usually undertaken when myocardial oedema precludes closure and emergency opening of the sternum is usually undertaken for management of suspected cardiac tamponade.

6.2.3 Cardiac Surgery Protocol

General

All infants and children who undergo cardiac surgery are admitted to the PICU in the immediate post operative period except neonates undergoing ligation of an uncomplicated patent ductus arteriosus who are returned to the Neonatal Intensive Care Unit (NICU).

The operative team comprises staff, Fellows and Residents

in Cardiovascular Surgery and Anaesthesia. Observers and students from multiple disciplines may be present.

Children undergo a chlorhexidine bath the evening before elective surgery; the pre-operative patient care scrub consists of a 5 minute application of povidone iodine (Ford-Jones 1988). At induction of anaesthesia prophylactic cefazolin is administered intravenously in a dose of 40mg/kg body weight up to a maximum total dose of 750 mg. After establishment of cardiopulmonary bypass 40 mg. of cefazolin per 250 mls of prime solution are added to the pump. Post operatively the dose of antibiotic given at induction of anaesthesia is administered intravenously commencing 6 hours after the first dose and continuing every 6 hours to a total of 9 doses. In the case of penicillin allergy, vancomycin is given at induction of anaesthesia (but it is not used in the pump solution).

If a chest tube is in situ, or if the sternum remains open in the post operative period (either electively or following emergency re-opening), antibiotic is continued until the chest tube is removed or the sternum is closed. For children undergoing delayed sternum closure gentamicin 2mg/kg (max total dose 120mg) is also given 1 hour before sternum closure and every 8 hours thereafter for 72 hours.

Dressings on chest tubes and open sternotomy wounds include a sterile waterproof bandage (Surgihesive, Squibb(R),

Montreal Canada) for 3 days followed by transparent semipermeable membranes (Opsite$^{(R)}$) for 4 days if the child stays in the PICU. A closed sternotomy wound is left uncovered. Chest drains and pacemaker wires are removed aseptically. PICU policy with respect to dressings and care of incision site, pacemaker wires, chest tube sites etc. is detailed in Appendix 3.

Intravascular Lines

Most intravascular lines are placed while in the operating room as a sterile procedure either percutaneously by anaesthetists or by surgeons by means of a cut down. Arterial lines are placed in the radial, femoral or dorsalis pedis arteries. Percutaneous central venous lines are placed in the internal jugular, subclavian, basilic or femoral veins. Umbilical lines inserted in the neonatal intensive care unit (NICU) are not used for monitoring. Intravascular Lines are maintained as per PICU policy based on CDC guidelines - see Appendix 2. Policies with respect to arterial line and central venous line dressings are detailed in Appendix 2.

Measurement of Cardiac Output

Pulmonary artery flotation catheters (Swan-Ganz catheters) are not routinely used in cardiac surgery patients. Cardiac output is routinely measured using the indocyanine

green method. Dye is usually injected into a central venous line and blood is sampled via the arterial catheter. In certain circumstances direct right atrial (RA), left atrial (LA) or pulmonary artery (PA) catheters may be left in situ post operatively.

Fluids/Nutrition

Initial fluid management at 75% maintenance during ventilation includes crystalloid and blood products as required. Nasogastric feeds are resumed as soon as possible. Total parenteral nutrition is reserved for children deemed to require a high calorie intake or those who have intolerance of nasogastric feeds after more than 5 days.

6.2.4 Patient Follow-up

All patients were followed, by the Research Fellow, for development of wound infection and infection at other sites during their stay in the PICU and for 72 hours after transfer to the open cardiology ward as per general methodology. In addition patients were followed for at least two months for the development of wound, chest tube and pace-maker wire site infections. This follow-up was carried out by the Infection Control Nurse.

6.2.5 Data Analysis

The nosocomially infected patient ratio (NIPR) was calculated by obtaining the total number of patients who acquired one or more infections following cardiac surgery by the number of patients undergoing surgery and admitted to the PICU x 100.

The nosocomial infection ratio (NIR) was calculated by obtaining the total number of infections following cardiac surgery by the number of patients undergoing surgery and admitted to the PICU x 100. The proportion of infected and uninfected patients was compared using the two tailed Fisher exact test. The information was not computerized in a manner which allowed for multiple correlation analysis.

6.3 RESULTS

Three hundred and ten patients underwent cardiac surgery between July 1st 1987 and 29th February 1988. The wound infection ratio was 12.9 and the NIR was 25.2. The wound infection ratio was 8.0 for patients undergoing closed (non cardio-pulmonary CPB) surgery and 6.7 for those undergoing open (cardio-pulmonary CPB) surgery - see Table 12.

Of 87 patients undergoing closed (non CPB) surgery, 11 patients developed 7 wound infections and 7 non wound

infections (1.3 per patient). Of 223 patients undergoing open (pump) surgery, 29 patients developed 15 wound infections and 49 non wound infections (2.2 per patient).

Table 12 Incidence of post operative wound infection by category of cardiac surgery (open or closed)

	Total no of procedures	Open	Closed
No patients	310	223	87
No wound infections	22	15	7
Incidence wound infections	7.1	6.7	8.0
No wound infections	56	49	7
Total incidence infections	25.2	28.7	16.1

Open (cardiopulmonary bypass (CPB)) and closed (non cardiopulmonary bypass (non-CPB)) cardiac surgery procedures are defined in Appendix 6.

6.3.1 Characteristics of Infections Following Closed (Non-CPB) Surgery

A total of 87 patients underwent closed cardiac surgery. Condition as measured by the PRISM score at the time of admission to the PICU after Surgery included 55% with a PRISM score <10 and 45% with a PRISM score ≥10.

Infection at all sites

Of the patients with a PRISM score <10 8.3% (4/48) developed infections at any site. Of the patients with a PRISM score ≥10 17.9% (7/39) developed infections at any site ($p > 0.05$. NS). Infections included four bacteraemias (two of unknown aetiology; one secondary to a tunnelled central line; and one secondary to an arterial line) of which three were caused by coagulase negative staphylococci and one was caused by Pseudomonas aeruginosa. The other three infections were at the following sites : eye (Strept. viridans), skin (P. aeruginosa), and chest tube site (no isolate). These infections had a mean onset of 6.1 days post operatively (median 6 day).

Wound Infection

Of the patients with PRISM scores <10, 6.3% (3/48) developed wound infections compared to 10.3% (4/39) of patients with a PRISM score ≥10 ($p > 0.05$. NS). The

incidence of post operative wound infection by p3rocedure is shown in Table 13.

No post operative wound infections occurred in the two months following sternal closure, cardiac trauma, pacemaker insertion, Glenn anastomosis, Blalock-Hanlon septectomy or other septostomy, innominate artery suspension, PA banding, plication of diaphragm, thoracotomy, and vessel repair procedures.

Post operative wound infections occurred in the two months following pectus excavatum repair, central shunt, PDA ligation, pericardial drain insertion, Blalock-Taussig shunt and repair of coarctation of the aorta. The wound infection onset was a mean of 12.1 days (median 13 days) after surgery. The causative agents were Staphylococcus aureus 70% (5/7) and coagulase negative staphylococci 30% (2/7).

Table 13 Post Operative Wound Infection Following Closed (Non CPB) Surgery

Procedure	% infected	(n infected)
pectus excavatum repair	100%	(1)
central shunt	33%	(1)
PDA ligation *	33%	(1)
pericardial drain insertion	14%	(1)
Blalock-Taussig shunt	7%	(2)
coarctation of aorta repair	5%	(1)

* Post operatively, neonates who undergo ligation of an uncomplicated PDA are routinely admitted to the Neonatal Intensive Care Unit (NICU)

6.3.2 Characteristics of Infections Following Open (CPB) Surgery

Condition as measured by the PRISM score at the time of admission to the PICU after surgery included 38% with a PRISM score <10 and 62% with a PRISM score ≥10.

Infection at all sites

Of the patients with a PRISM score <10 10.6% (9/85) developed infections at any site. Of the patients with a PRISM score ≥10 17.4% (24/138) developed infection at any site (p >0.05. NS). Infections included 4 bacteraemias of unknown primary source, 8 non-tunnelled central line infections, 5 arterial line infections, 10 chest tube site infections, 7 lower respiratory tract infections, 5 urinary tract infections, 4 eye infections, 3 skin infections, 3 peritoneal drain infections / peritonitis. The 8 infections in percutaneous jugular central venous lines occurred in lines in place a median of 8 days (range 1-10 days). The 5 arterial line infections occurred in arterial lines in place a median of 11 days (9-20 days).

Wound Infection

No patients with a PRISM score <10 developed post operative wound infections. Of patients with a PRISM score ≥10, 10.9% (15/138) developed wound infections (p >0.05 NS).

Post operative wound infection by operative procedure is shown in Table 14. No post operative wound infections occurred in the two months following Mustard Procedure, valve (mitral/aortic) replacement, Rastelli procedure, valvuloplasty, pulmonary arterioplasty, RVOT obstruction repair and repair of sub aortic stenosis.

Post operative wound infections (including 3 cases of mediastinitis), followed double outlet right ventricle repair, truncus arterisosus repair, switch procedure, valvotomy, cardiac conduit insertion, transverse collaterals repair, Fontan procedure, AVSD repair, VSD repair, ASD repair and Tetralogy of Fallot repair. Wound infection onset time was a mean of 9.7 days (median 10 days) after surgery. The causative organisms included singly or in combination; coagulase negative staphylococci 33% (5/15), Pseudomonas aeruginosa 27% (4/15), Candida species 27% (4/15). Staphylococcus aureus 20% (3/15) and each of Acinetobacter sp. enteric streptococcus and Streptococcus viridans 7% (1 each). Mediastinitis was caused in 3 cases by P. aeruginosa, and in one case by Candida sp.

Table 14 Post operative wound infection following open (CPB) surgery

Procedure	% infected	(n infected)
double outlet right ventricle	25%	(1)
truncus repair	20%	(1)
switch	17%	(2)
valvotomy	17%	(1)
conduit insertion	13%	(2)
other (repair of transverse collaterals)	13%	(1)
Fontan	7%	(2)
AVSD repair	6%	(1)
VSD repair	6%	(2)
ASD repair	4%	(1)
Tetralogy of Fallot repair	4%	(1)

6.3.3. Wound Infections in Patients with Open Sternum (Elective or Emergency)

27.6% of patients in whom the sternum was either electively left open after surgery or re-opened as an emergency procedure in the PICU, developed wound infection. There was no difference in the rate of wound infection following elective or emergency opening (5/18 vs 3/11, $p > 0.05$ NS).

Three cases of mediastinitis occurred in 29 patients (10.3%) where the sternum was open post operatively. In patients where the sternum was at no time open post operatively 4.6% (13/281) developed post operative wound infection ($p = 0.00028$) see Table 15.

Table 15 Incidence of post operative wound infection in cardiac surgery patients with open sternum (elective or emergency) in the post operative period

	Open Sternum		Other cases
	elective	emergency	
No. of patients	18	11	281
No. wound infections	5	3	14
Wound infection ratio	27.8	27.2	5.0

($p = 0.00028$, open sternum vs other cases)

6.3.4 Summary of Nosocomial Infections

The relative frequency of nosocomial infection by site, in cardiac surgery patients is listed in Table 16.

In proportional frequency, the incidence of bacteraemia (including central line and arterial line infections) of (27%) equalled wound infections (28%). The most common isolates were coagulase negative staphylococci (30%), P. aeruginosa (21%), S. Aureus (16%) and Candida sp. (15%). No viral illness was identified clinically.

The relative frequency of organisms causing infection is detailed in Table 17.

Table 16 Relative frequency of nosocomial infection by site in cardiac surgery patients

Site	No.	% of all nosocomial infections
wound	22	28%
Bacteraemia 1°,no source	6	8%
Central Line bacteraemia (+/- site)	9	11%
Arterial Line bacteraemia (+/- site)	6	8%
Chest tube/pacer wire site	11	15%
Lower respiratory	7	9%
Urine	5	6%
Eye	5	6%
Skin	4	5%
Peritoneal drain/peritonitis	3	4%
Gastrointestinal	0	0
Upper respiratory	1	1%
TOTAL	78	100%

Table 17 Relative frequency of organisms causing nosocomial infections in cardiac surgery patients

Organism	No.	Proportional % of all organisms
Gram Positive Bacteria		
Coagulase negative staphylococci	24	30%
S. Aureus	13	16%
group D streptococcus	2	2.5%
Branhamella Catarrhalis	1	1.3%
S. viridans	1	1.3%
diphtheroids	2	2.5%
Gram Negative Bacteria		
Pseudomonas aeruginosa	17	21%
Escherichia coli	0	
Proteus mirabilis	0	
Enterobacter cloacae	4	5%
Acinetobacter sp.	1	1.3%
Klebsiella sp.	1	1.3%
Pseudomonas putida	1	1.3%
Haemophilus influenza	1	1.3%
Fungus		
Candida sp.	12	15%
TOTAL	80	100%

6.4 DISCUSSION

This work further defines the epidemiology of infection, following cardiac surgery, by providing procedure specific infection rates in patients whose severity of illness is scored using the PRISM scoring index. Open sternum and high PRISM scores were clinically and statistically associated with higher infection rates. The predominant pathogens differed according to procedure. Coagulase negative staphylococci, Pseudomonas aeruginosa and Candida sp. were important pathogens in open (CPB) cases. (Candida sp. has previously been reported to cause only 6% of median sternotomy infections. (Edwards 1983)). In contrast, staphylococci predominated in closed (non CPB) cases.

The high proportion (27%) of intravascular line related bacteraemias and line exit site infections is noteworthy because of the underlying heart disease which makes these patients vulnerable to endocarditis. These infections are generally, considered to be preventable by adherence to strict aseptic technique during insertion and maintenance of lines and their prompt discontinuation after a maximum of 5 days of placement. Difficult vascular access and unstable condition of the patient may necessitate the prolonged use of individual lines - in this series infected percutaneous central and arterial lines were in place a median of 8 and 11 days respectively.

The wound infection rate in this series is somewhat higher than is expected from other paediatric and adult series. (Edwards 1983) (Fisher 1981) (Archer 1983) (Dandalides 1984) (deSilva 1984) (Steffenson 1987) (Flynn 1987) (Kaiser 1984) (Simchen 1983) (Farrington 1983) (Yonkman 1984) (Williams 1983) (Bor 1983) (Hoffman 1981) (Weinstein 1976) (Voiriot 1987) (Kernodle 1988) (Wilson 1988) (Wray 1973).

10.7% of patients who were sicker on admission to the PICU as measured by a PRISM score $\geq$10 acquired infection vs 2.3% of those with PRISM scores <10. Indeed the rate is higher than in the period from 1984 to 1986 inclusive at this hospital when overall post operative wound infection rates for cardiac surgery patients (infections per 100 admissions) ranged from 1.1 - 1.7 for the 708 - 814 procedures carried out per year (unpublished data).

In the Hospital for Sick Children, Toronto, from January 1983 till July 1985 the total cardiac infection ratio (including wounds) was 4.7 which is lower than neurosurgery (13.1), general surgery (11.2), neurology (9.1), renal (7.4), ENT (5.8) and general paediatrics (5.7) (Milliken 1988). In these earlier studies surveillance was carried out by the Infection Control nurses using twice weekly chart review and daily review of microbiologic reports. It is not possible to know if the current higher rate is due to higher intensity surveillance by the full time research fellow in association with the use of the nursing sentinel

sheet system; sicker patients as measured by the PRISM score; the introduction of new procedures (e.g., elective delayed closure of the sternum); timing early in the academic year; or other unmeasured factors.

Previous surveys have involved health record reviews over prolonged periods of time and may underestimate infection rates. It is believed that the intensity of surveillance in this survey probably surpasses that of previous surveys.

While the severity of wound infection differed among patients, there was consensus between the PICU and cardiac surgery staff on the presence of wound infection; stitch abscesses were not identified and cases of non union/delayed union of the sternum without pus were deemed insufficient for a diagnosis of wound infection to be made. In any future study scoring of the severity of wound infection could be undertaken as suggested by Wilson et al (1988).

The PRISM score on return to the PICU after surgery clearly identifies a sicker population of patients at higher risk of infection than the uninfected group. Preventive intervention focussing on the indications for the sternum remaining open in the post operative period, designation of responsibility for administration of pre and intra operative antibiotics, duration of and monitoring of the pre-operative skin site prep and other operating room

procedures was co-ordinated through a series of meetings held by the staff of Cardiac Surgery, PICU and Infection Control during and after this study period. The early post operative wound infection ratio in the four month period since the end of the study and at the end of the academic year has decreased to 2.0 using the Infection Control Sentinel Sheet (ICSS) system of detection.

The origin of infection is not clear from this series. Edwards (1983) reported 9 children with median sternotomy infections (0.1%) including 3 with mediastinitis during a 12 year study period involving 6775 procedures. Risk factors in 6 patients included one or more of: a bypass time of greater than 1 hour, excessive post operative bleeding, low cardiac output for 24 hours or more post operatively, re-exploration for control of bleeding and inadequate antimicrobial prophylaxis.

The higher PRISM scores of our infected patients and the failure of any patients with a PRISM score <10 to develop wound infections following open surgery is another measure of a more difficult operative procedure in patients who developed infection in comparison to those who did not. While the difference in total nosocomial infection rates in patients with PRISM scores <10 and ≥ 10 did not reach statistical significance, either singly (by either open (CPB) or closed (non CPB) cases), or combined, the power to detect a difference was low. The infection rate was twice

as high in patients with a PRISM score ≥10 than those <10 (21.2 vs 9.8) and no wound infections occurred in the 85 patients undergoing open pump surgery with PRISM scores <10. The difference in wound infection rates was significantly different.

Others have attempted to trace cardiac infections to contamination of hands and bedside air, exposure to soiled utility sink aerosols (Dandalides 1984), surgery in the face of defective air handling system, and prolonged operative time (deSilva 1984). An outbreak of Pseudomonas maltophilia involving 8 of 13 children undergoing open heart surgery during a 95 week period was traced to contamination of both the calibration device used on the pressure monitoring system and the sensor surface of the transducers used in this system (Fisher 1981).

Edwards (1983) has summarised reports showing an inverse relationship between the incidence of wound infections and the number of procedures performed yearly, noting a rate of 2% when the number of procedures exceeded 600 (Culliford 1976) (Serry 1980) (Jurkiewicz 1980) increasing to almost 6% when only 17 procedures were performed yearly (Wray 1973). Meanwhile, Culliford (1976) identified infections in 0.4% of 227 children undergoing median sternotomy. While as a general statement this may be true, our experience clearly shows that high volume surgery does not

preclude an increased incidence of infection at least in some periods in time or the academic year.

The problem with most of the studies performed to date is that they employ case control analysis to identify risk factors for the development of wound infection. Correction of the purported risk factors is associated with a decline in infection rates. When multiple pathogens are involved as in this report it is doubtful that a cluster of post surgical wound infections is related to any single break in technique (Kaiser 1984).

Prospective stratification of risk factors of patients undergoing surgery using procedures and PRISM scoring on PICU admission represents a preliminary attempt to overcome this earlier problem. Further intensive prospective analysis of risk factors during endemic and epidemic periods could address in addition, surgical technique, operating room protocol and environmental factors although these may be extraordinarily difficult to quantify.

The tendency for deep mediastinal infections to be caused by Gram negative enteric pathogens is reiterated here (Edwards 1983) (Culliford 1976); all four cases in our series were caused by Pseudomonas aeruginosa and Candida sp. Similarly the onset of post operative wound infection has previously been reported to be 10 to 15 days post operatively (Edwards 1983) (Culliford 1976) (Serry 1980)

(Grmoljez 1975) and was in our study 13 days (median) for closed cases and 10 days (median) for open cases.

Apart from wound and intravascular line related infections other sites of infection are also important in these patients. One child in the current series went to the operating room with untreated candiduria and developed Candida sp. wound infection post operatively. Workers in the HSC have previously reported corneal opacity and unilateral blindness following nosocomial P. aeruginosa infection in a post operative cardiac patient who was subjected to large numbers of manoeuvres about the face (e.g., suctioning, nasogastric tube passage, endotracheal intubation). In a study by King corneal damage was reported in 7.4% of 30 paediatric patients with nosocomial Pseudomonas aeruginosa conjunctivitis (King 1988).

There is a high morbidity and mortality associated with respiratory syncitial virus (RSV) infection occurring in children with congenital heart disease associated with increased pulmonary blood flow. (McDonald 1982). These patients are significantly more likely to require care in the PICU including assisted ventilation and, are more likely to die than their counterparts without RSV infection.

CHAPTER 7

EVALUATION OF A NEW METHOD OF NOSOCOMIAL INFECTION SURVEILLANCE FOR USE IN THE PICU: THE INFECTION CONTROL SENTINEL SHEET.

EVALUATION OF A NEW METHOD OF DETECTION OF NOSOCOMIAL INFECTION IN THE PICU: THE INFECTION CONTROL SENTINEL SHEET

SUMMARY

To improve the efficiency of nosocomial infection detection in the Hospital for Sick Children, Toronto, a highly structured system, the Infection Control Sentinel Sheet (ICSS) has been developed. It combines initial reporting by the bedside nurse of patient symptoms possibly related to infection with patient follow-up by the Infection Control Nurse (ICN).

Between 1/7/87 and 29/2/88, in the PICU, a prospective study was undertaken which compared nosocomial infection data obtained through ICSS with data obtained by a full time Research Fellow (intensivist) performing daily bedside observation/and chart review. Ratios of nosocomial infections and nosocomially infected patients were 15.8 and 7.0 respectively among 685 admissions. (This included 5 infections identified only through the ICSS system so, in fact, the 'gold standard' became an amalgamation of the two systems). The sensitivities for detection of nosocomially-infected patients by bedside review and ICSS were 100% and 87% respectively. The sensitivities for detection of standard infections (blood, wound and urine) by bedside review and ICSS were 88% and 85% respectively. The

sensitivities for detection of nosocomial infections at all (11) sites by bedside review and ICSS were 94% and 72% respectively.

Infections missed by the ICSS were: minor (e.g., drain, skin, eye); uncertain/needed physician diagnosis (e.g., otitis media, pneumonia); not requested on the ICSS (e.g., URI); related to follow-up of deceased patients or minor mis-classifications / failure to associate with a device (e.g., central line related).

Daily PICU surveillance by the ICN required only 20 minutes per day. The ICSS appears to be a highly promising system which has many unmeasured benefits.

7.1 INTRODUCTION

Early and complete detection of nosocomial infection is essential in order to initiate preventive intervention and reduce transmission. This applies in particular to post operative pneumonias and urinary tract infections (Haley 1985a). Surveillance methodology has recently been reviewed by Abrutyn (1987) and is summarized in Table 2. Currently used methods have numerous disadvantages - they are labour intensive or insensitive, or dependent on systems not available in all hospitals e.g., Kardex system (Wenzel 1976a).

At the present time, there are many new demands on Infection Control personnel which reduce time available for data collection. These include education about AIDS, new procedures and products, interpretation of commensal organisms which may be pathogens in the critically ill or immunocompromised patient, recognition of nosocomial viral syndromes and identification of infection in sicker patients in association with new devices and procedures.

To provide more time for the forementioned activities, and to heighten interest in nosocomial infection, the responsibility for detection of infected patients (not differentiating between community and nosocomial infections) was shifted to the bedside night nursing staff through an Infection Control Sentinel Sheet System (ICSS),

an adaptation of a system initiated elsewhere (personal communication C. Andrews, Columbus, Ohio).

Table 2 Sensitivity of methods of case-finding for nosocomial infection

Method	Reference	Sensitivity
physician self report forms	Eickhoff 1969	0.14 - 0.34
fever	Wenzel 1976 (a)	0.47
antibiotic use	Wenzel 1976 (a)	0.48
fever + antibiotic use	Wenzel 1976 (a)	0.59
microbiology reports	Eickhoff 1969 Wenzel 1976 (a) Thoburn 1968 Haley 1980 (b)	0.33 - 0.65
selected chart review using 'Kardex' clues	Wenzel 1976 (a)	0.85
total chart review	Wenzel 1976 (a)	0.90
Boston City Hospital method (bedside exam)	Kislak 1964	1.00
prospective chart review	Haley 1980 (b)	0.52 - 0.90
SENIC pilot retro-spective chart review	Haley 1980 (b)	0.66 - 0.80
standard (bedside exam)	Freeman 1981 (a)	1.00**

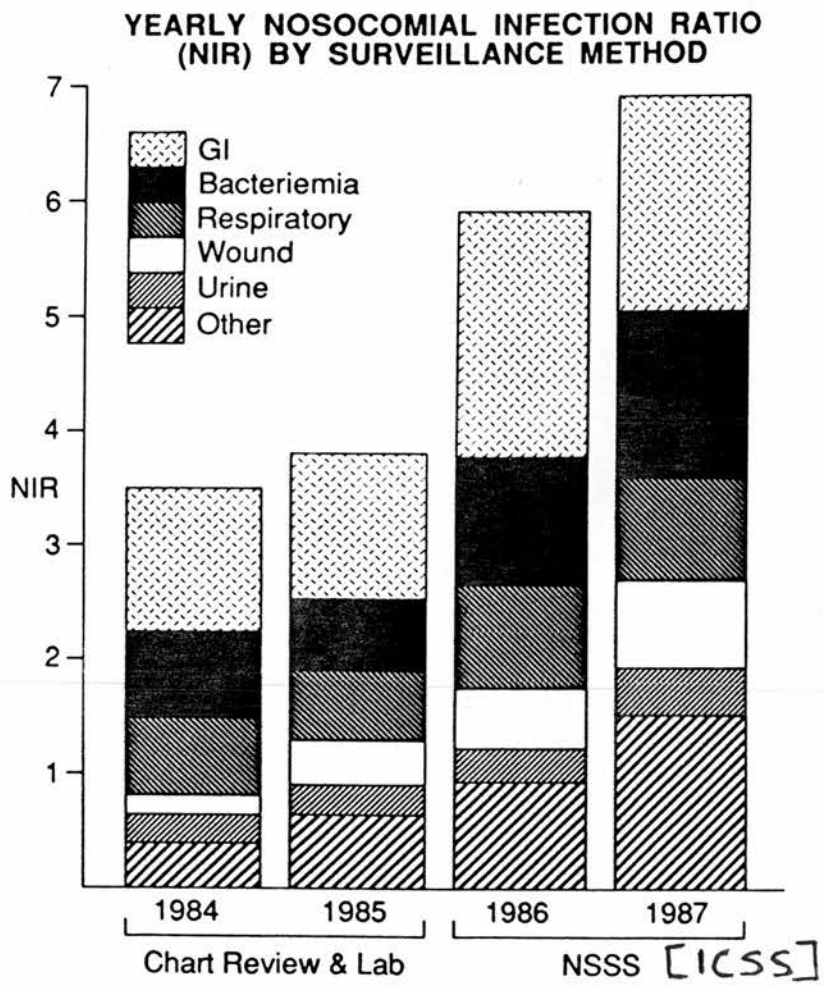
(Adapted from Freeman 1981 (a) and Thompson 1987).

** by definition, all other sensitivities are referable to this standard.

The use of the ICSS hospital-wide during 1986-1987 was associated with a 50% increase in the incidence of reported nosocomial infections compared to the previous 2 years when weekly chart review and daily lab rounds were undertaken. See Figure 6.

To determine the sensitivity of the new surveillance strategy, a prospective study was carried out in the Paediatric Intensive Care Unit comparing the results of the ICSS system with results obtained by a Research Fellow (intensivist) independently carrying out nosocomial infection surveillance by means of daily bedside observation and chart review.

Figure 6 HSC, Toronto: yearly nosocomial infection ratio (NIR) by surveillance method.



7.2 METHODOLOGY

7.2.1 General

The study was performed in the setting and using the general methods as described in Chapter 4. To detect nosocomial infection, a Research Fellow carried out daily bedside examination of all patients as well as in-patient chart review as per general methodology. At the same time the PICU continued routine use of the Infection Control Sentinel Sheet (ICSS) under the supervision of the Infection Control Nurse (ICN).

7.2.2 Definition of the Infection Control Sentinel Sheet System (ICSS)

The sentinel sheet was developed and pretested on samples of convenience; minor revisions for clarity and acceptability were made in 1985 and the system was introduced hospital-wide in January 1986. In The Hospital for Sick Children, Toronto, the Admitting Department produces the sentinel sheet at 7 p.m. and delivers it to the PICU at 2 a.m. along with the ward census sheet. The sentinel sheet consists of the names of each patient on the ward with a check list of symptoms of infectious diseases (fever, cough etc.,). A sample sentinel sheet is detailed in Figure 7. Each bedside nurse 'flags' symptoms present in his/her patient.

Figure 7 Contents of the Infection Control Sentinel Sheet (ICSS)

THE HOSPITAL FOR SICK CHILDREN
INFECTION CONTROL

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WARD INTENSIVE CARE

PATIENT NAME / ADMIT DATE	TEMP	INCISION LINE	SEPTIC WORK UP	IV/SITE PROB	URINE	DIARRHEA	ISOLATE	CENT LINE/ SITE PROB	CHESTTUBE (SITE)	
CHILD ONE 19-08-88	( )	( )	( )	( )	( )	( )	( )	( )	( )	_____
CHILD TWO 23-08-88	(✓)	(✓) reddened + draining	( )	( )	( )	( )	( )	( )	( )	_____
CHILD THREE 25-08-88	( )	( )	( )	( )	( )	( )	( )	( )	( )	_____
CHILD FOUR 23-08-88	(✓)	( )	(✓)	( )	( )	( )	( )	( )	( )	antibiotics started
CHILD FIVE 23-08-88	( )	( )	( )	( )	( )	( )	( )	( )	( )	_____
CHILD SIX 25-08-88	( )	( )	( )	( )	( )	( )	( )	( )	( )	_____
CHILD SEVEN 23-08-88	( )	( )	( )	( )	( )	(✓)	(✓)	( )	( )	_____
CHILD EIGHT 24-08-88	( )	( )	( )	( )	( )	( )	( )	( )	( )	_____
CHILD NINE 24-08-88	( )	( )	( )	( )	( )	( )	( )	( )	pus at site (✓)	swab sent for C&S

SIGNATURE: C. Jones RN

Differentiation between community and nosocomial infections is not required on the ICSS system. The completed ICSS is signed by the Charge Nurse at the end of his/her shift and is placed in a box in the PICU; sheets are collected daily at approximately the same time in the morning from Monday to Friday by the ICN. On Monday, sheets for the previous Friday through to the Sunday are collected. During absence for sickness/holidays the sentinel sheets are saved and given to the ICN on her return. The remainder of the process constitutes the ICSS.

Patients, identified on the sheet as having symptoms or signs of infection, are discussed by the ICN with the charge nurse or responsible nurse. Flow sheets and medical records are reviewed by the ICN and if a nosocomial infection is confirmed, a detailed surveillance report is completed for computer entry to the nosocomial infection data base. In addition to the sentinel sheet, the system includes correlation of specific microbiology results by the ICN. All positive blood, CSF, peritoneal fluid and joint aspirate cultures as well as multiple resistant organisms are recorded on a computer print out sheet in the laboratory and are available to the ICN each morning. Wound, eye and skin culture reports are compiled manually for daily pick up. Enteric and respiratory viral specimen results are reviewed twice daily. Clostridium difficile toxin and hepatitis B serology are reviewed daily. A

monthly print-out of all positive viral specimens is provided for the ICN by the Virology department.

If a nosocomial infection is confirmed, a surveillance report is completed by the ICN. Surveillance reports are verified weekly by the Infection Control Physician and a computerized report is returned to the PICU Nursing Unit Administrator and the PICU Director the following month. The sentinel sheet had been in use in the PICU for the 18 months prior to the study. The sentinel sheet is introduced to and reviewed with new staff by clinical instructors and the ICN at their respective ward nursing orientations.

7.2.3 Data Entry

ICSS data from the routine surveillance were entered and analyzed on Apple IIe using an Infostar System(R) (micropro International Cord) data base programme. Data from the bedside observation and chart view exam were managed by the Research Fellow independently of the ICSS and Infection Control Programme and were batch entered for each patient after discharge.

7.2.4 Data Analysis

Infections were reported as Nosocomial Infected Patient Ratio (NIPR) and as Nosocomial Infection Ratio (NIR).

$$\text{NIPR} = \frac{\text{no. of infected patients}}{\text{no. of admissions}} \times 100$$

$$\text{NIR} = \frac{\text{no. of infections}}{\text{no. of admissions}} \times 100$$

The 'gold standard' was determined by amalgamating the number of infections identified by bedside observation/chart review (BSO/CR) and the ICSS. Results obtained from each system were compared to determine sensitivity. No attempt was made to exclude infections identified by either system from the pool of infections forming the 'gold standard'. Specificity could not be calculated reliably because patient identification in the ICSS included community acquired infections.

7.3 RESULTS

7.3.1 Prevalence of nosocomial infection

685 patients were admitted during the 8 month study period; 108 infections were identified in 48 patients (NIPR = 7.0, NIR = 15.8). This total includes 7 infections identified

through the ICSS but not identified through bedside observation (secondary bacteraemia, skin infection, urinary tract infection (3 cases), infected chest drain site and superficial post operative wound infection).

7.3.2 Sensitivity in detection of infected patients

BSO/CR identified all infected patients. The ICSS detected 40 of 46 (87%) of infected patients. This included 15/20 (75%) of patients with single infections and 25/26 (96%) of patients with 2 or more sites of infection (see Table 18).

Among those patients with a single infection who were not detected by the ICSS, the infections included pneumonias (2), conjunctivitis (2), and otitis media (1). The only patient with multiple infections who was not identified by the ICSS had a mixed bacteraemia with Micromuciliginosis sp. in a peripheral blood culture and alpha haemolytic streptococci in a central line blood culture.

Table 18 Comparative sensitivity in the detection of infected patients: Infection Control Sentinel Sheet v bedside observation.

Patients	Sensitivity of system	
	ICSS*	BSO / CR**
all infected patients	0.87	1.00
patients with 1 infection	0.75	1.00
patients with >2 infections	0.96	1.00

* ICSS = Infection Control Sentinel Sheet System

** BSO/CR = bedside observation / chart review

The ICSS identified 80% or more of infections at the following sites (see Table 19): arterial line (100%), GI (100%), wound (93%), CVL (86%), bacteraemia (83%). Respiratory and superficial/minor (drain, eye, skin) infections were inconsistently identified. BSO/CR included daily chest X-ray review while the ICSS did not. Upper respiratory infections were not listed on the ICSS because of the difficulty in interpreting symptoms in the intubated patient; those infections missed were physician diagnosed (1 case of herpes glossitis, 3 cases of otitis media).

There were problems verifying infections (14 cases) in patients identified on the ICSS. Reasons included the following:-

1) chart unavailable (1 patient with 1 each of bacteraemia, central line infection, arterial line infection, wound infection and urinary tract infection).
2) misclassification
   arterial line infection (2) misclassified as blood
   wound (1) misclassified as skin
   drain (1) misclassified as wound.
3) dismissal of pathogen as a contaminent in: central line (1); arterial line (1); urine (1).
4) failure to recognize multiple episodes of infection occurring within a short period of time (central line infection at each of jugular/arm sites within a 72 hour period (2 cases).

Table 19 Comparative Sensitivity by method and site of infection: Infection Control Sentinel Sheet v bed-side observation.

Site	(no. detected by gold standard)[1]	Sensitivity of BSO/CR[2]		Sensitivity of ICSS[3]	
			(no.)		(no.)
bacteraemia	(12)	92%	(11)	83%	(10)
CVL	(14)	100%	(14)	86%	(12)
arterial line	(12)	100%	(12)	100%	(12)
wound	(14)	93%	(13)	93%	(13)
resp. upper	(7)	100%	(7)	43%	(3)
resp. lower	(12)	100%	(12)	42%	(5)
urine	(14)	79%	(11)	79%	(11)
GI	(1)	100%	(1)	100%	(1)
eye	(5)	100%	(5)	40%	(2)
drain	(14)	93%	(14)	64%	(9)
skin	(3)	67%	(2)	33%	(1)
TOTAL	(108)	94%	(102)	73%	(79)

1 gold standard - amalgamation of all infections identified by daily bedside observation and the Infection Control Sentinel Sheet system

2 bedside observation / chart review by Research Fellow

3 Infection Control Sentinel Sheet System (ICSS) - flagging by bedside nurse on night shift.

7.3.4 Measured benefits of Infection Control Sentinel Sheet over bedside examination.

Additional infections and additional microbes were identified. As noted above, seven additional infections were identified through the ICSS, but not through the BSO/CR. Five additional organisms reported by the ICSS system include two S. aureus (wound related), 2 coagulase negative staphylococci (wound, chest drain related), and 1 pseudobacteraemia (Pseudomonas putida (Simor 1985)), as well as the isolates associated with the forementioned 7 sites, a total of 13 organisms.

7.3.5 Unmeasured benefits of Infection Control Sentinel Sheet

The time spent in the PICU each day for: collection of the ICSS, review of flagged patients and completion of a data entry sheet is 20 minutes. Additional unmeasured time is spent on daily lab rounds and occasionally in the Health Records Department reviewing charts of patients who were unavailable on the ward but flagged on the ICSS.

The ICSS facilitates correlation with findings on microbiology laboratory surveillance.

The system involves bedside nurses and charge nurses who know the patient best; it may heighten their awareness of

infection and their interest in its prevention. It reduces time spent on surveillance by the ICN and makes more time available for the other functions of the ICN, especially teaching. It facilitates regular ward interaction, heightens awareness of nosocomial infections and provides an opportunity to review isolation of patients with both community acquired and nosocomial infections.

7.3.6 Biases

Biases acting to underestimate the sensitivity of the ICSS include the broad spectrum of infectious events and attribution of infections to devices. Additional care must be taken to identify the sampling site and line to provide this latter service. Also diagnoses not clearly listed on the sentinel sheet were included in the gold standard e.g., otitis media, URTI. Comparison to sustained, period prevalence surveys more commonly used to determine sensitivity.

The time dedicated by the intensivist (3 hours per day) to this study makes BSO/CR underreporting and overestimation of the ICSS unlikely. While the Hawthorne effect could be improving use of the ICSS, the system had been in place for 18 months prior to study and the research fellow had been working as a clinical fellow in the PICU the previous year so that there was little obvious change in the PICU during the study period.

7.4 DISCUSSION

The ICSS provides a method which is complete, concurrent, efficient and simple. It provides the opportunity for close interaction with nursing staff and shifts ICN responsibility from case finding to case verification. Surveillance activities have been defined as active, if Infection Control personnel perform case-finding, and passive, if dependent on reporting care givers. There are several unique features of this active system which differentiate it from a passive system. Unique characteristics include:

1) daily computerized list of ward patients and symptoms of infection
2) nightly delivery of ICSS to ward by Admitting Department staff
3) night nurse 'flags' symptoms present in her patients; differentiation between community and nosocomial infections is not required
4) night nurse and charge nurse 'sign off' the ICSS
5) scheduled daily 'pick-up' of ICSS in the morning by the ICN
6) review of 'flagged' patients by ICN

The implementation of this system hospital wide, in 1986, resulted in approximately a 50% increase in reported nosocomial infection in the two year period during which

concurrent chart review on each ward (PICU, NICU twice weekly; others weekly) by the ICN was combined with daily laboratory result review. See Figure 9.

The ICSS is highly sensitive identifying 87% of infected patients, 75% of patients with a single infection and 96% of patients with two or more infections. The sensitivity testing undertaken here was particularly rigorous. The 'gold standard' included daily surveillance by a trained intensivist for the eight month period rather than point prevalence surveys by physicians; infections at 11 sites rather than only the four major sites (blood, urine, wound, lower respiratory) were sought, and attribution of infection to particular indwelling devices was attempted.

Sensitivity can be improved relatively easily, if staff agree on what they want reported. For example; diagnoses of bacteraemia can be clarified to include all pathogens, greater care can be taken in specimen collection in suspected IV related infection and ICN review of blood cultures and chest x-ray review of films with the unit radiologist can be added. In general, problems relate to interpretation of purported pathogens, completeness of culturing, limitations of clinical diagnosis and availability of charts/patients for review, all of which must be dealt with in a limited period of time. Collection of blood specimens through lines by bedside nurses with omission of peripheral blood cultures, in patients with

difficult access requiring sampling by a physician, makes the diagnosis of line-related infection difficult.

Respiratory infections were the only site of major importance not detected by this system. The poor sensitivity in detecting lower respiratory infections could be improved through systematic review of x-rays, although the difficulty in diagnosing pneumonia in the ventilated patient is well known. It is possible that the occurrence of these infections was over-reported by the dedicated intensivist. Other diagnoses such as otitis media and sinusitis are particularly dependent on the assiduousness of case finding and application of diagnostic tests.

It is of interest that the so called 'gold standard' of bed side review was not 100% sensitive in detecting infections at all sites at least over a prolonged period of time (8 months).

Surveillance needs in the 1980's have evolved substantially with the recognition of serious viral infections, particularly in paediatric patients and with a sicker paediatric patient population subjected to numerous invasive procedures. Comprehensive surveillance including all sites and associations with indwelling devices is required to identify problems in a PICU and at present no efficient surveillance system exists which adequately

fulfils these criteria in the limited time available to Infection Control personnel.

These data were collected in twenty minutes per day on the ward (and routine laboratory rounds) from trained bedside nurses in a unit which had been using the system for 18 months. The unique setting in which this study was undertaken should be appreciated. The PICU had a well developed Infection Control programme including previous research; the ICN was well known to the staff as was the ICSS; a strick schedule of delivery, completion and pick-up of the ICSS was adhered to.

Finally, underreporting is an important problem in any passive surveillance system, although it varies with the illness involved. Passive systems depend on non-Infection Control personnel who: understand definitions, apply definitions consistently, are aware of the need to report infection, and are willing to do so. Infection Control personnel then perform a verification function (Abrutyn 1987). According to Hoffher (1979), specific problems previously associated with an insensitive physician based ward reporting system, which it is believed have been addressed here, include: primitive and fragmentary classification of infections; definitions not standardised; time consuming completion of another chart sheet; retrospective case finding; self incriminating; information not co-ordinated by one person.

This detection system appears very promising and worthy of further study. It creates an environment conducive to the exchange of information about infection control while allowing for efficient detection of infected patients (Andrews 1988).

CHAPTER 8

ADVERSE SEQUELAE OF NOSOCOMIAL INFECTION IN THE PICU

ADVERSE SEQUELAE OF NOSOCOMIAL INFECTION IN THE PICU

SUMMARY

The incidence of certain events, judged by PICU personnel to be of adverse clinical significance, and which occurred as a direct consequence of nosocomial infection, was reported prospectively in the PICU population over a period of 8 months. During the study period 685 patients were admitted; 48 patients developed one or more nosocomial infections. Antibiotic treatment was indicated in 36 infected patients (75%); other adverse events (removal of a therapeutic device; cancellation or delay of surgery; extra surgery; isolation; readmission to PICU) occurred in 20 patients. A crude costing study of antibiotic required for treatment of nosocomial infection suggested that the minimum drug cost for 100 nosocomial infections was Can$ 15,000 (approximately £7,500). Mortality rates in infected and uninfected patients did not vary significantly.

8.1 INTRODUCTION

Traditional associations of nosocomial infection with sequelae such as increased mortality, increased morbidity and increased length of stay/patient care expenditure are limited since results are affected by the confounding effects of multiple uncontrolled variables.

With regard to mortality; care must be taken when attributing death to nosocomial infection since multiple factors such as birth weight and underlying illness make substantial contributions to mortality in the same population. (Goldmann 1983). In adult ICU patients, using the technique of step-wise logistic regression analysis, a positive association between nosocomial infection and mortality has been demonstrated (Craven 1988). This technique, however, has not been applied in studies of paediatric ICU patients, and in this group, it remains unclear whether mortality in nosocomially infected patients reflects causality or merely identifies a more severely ill group of individuals. (Brown 1987).

There have been efforts to derive increased patient care expenditure in adult patients, by estimating prolongation of hospital (or ICU) stay as a result of nosocomial infection. (Craig 1984) (Freeman 1979). Prolongation of stay is assessed by means of a matched cohort study or else by using the subjective estimates of physicians. There are

associated difficulties: adequate numbers of matched controls may be hard to find; both matched studies and subjective estimates are subject to the confounding effects of multiple uncontrolled variables. Estimates vary depending on whether the study is incidence or prevalence in type.

Problems abound when one attempts to associate nosocomial infection and morbidity not least of all because of a lack of meaningful, descriptive terminology with which to describe morbidity. Terms, traditionally used in paediatric patients, e.g., ' loss of school days', 'days not up to the play room', etc., are not relevant in the acute environment of the PICU. In critically ill patients there is a complex interaction between biological disease of individual body systems and the patient as a whole. Hence it may be impossible to distinguish accurately, between the biological sequelae of nosocomial infection and biological features of the underlying disease. The issue is further complicated by the fact that critically ill children exhibit an extremely wide range of pathology and age related response to illness.

To date, there has been no formal assessment of the adverse sequelae of nosocomial infection in the PICU though the literature does contain isolated reports both of fatalities and of increased expenditure attributable to

specific nosocomial infections in paediatric patients. (McDonald 1982) (Mufson 1973) (Pinner 1982).

Since associations of nosocomial infection and commonly accepted outcomes have so many limitations, an alternative approach has been sought. This is to select a number of specific events which are judged, from a clinical standpoint, to be of adverse significance, and then observe the incidence of these events as a direct consequence of a nosocomial infection.

The aims of this study were:-

1) to observe the incidence of certain clinical events (unscheduled surgery, cancellation or delay of surgery, removal of a therapeutic device, days of isolation, re-admission to the PICU, antibiotic use) as a consequence of nosocomial infection.

2) to undertake a crude costing study of antibiotic required for the treatment of nosocomial infection.

3) to report mortality rates in nosocomially infected and non infected patients.

8.2 METHODOLOGY

8.2.1 General

The study was performed in the setting and using the common methods as described in Chapter 4.

8.2.2 Adverse Clinical Events

Following discussion with PICU physicians and nursing staff, certain clinical events were selected, each of which was considered to be an adverse effect of a nosocomial infection. The event had to occur solely because of nosocomial infection; if there was doubt in respect of this, then the occurrence of the event was disregarded. The incidence of events was documented for each infected patient and entered on Data III collection sheet (Figure 8). The following events were chosen for use in the study:-

1) any type of isolation (complete room isolation; skin or wound precautions) required specifically because of nosocomial infection.

2) cancellation of surgery - any episode where anticipated surgery was cancelled or delayed specifically because of nosocomial infection.

3) removal of a therapeutic device specifically because of nosocomial infection. This did not apply to devices which were removed for some other reason (e.g., not functional, not required) and thereafter found to be infected.

4) extra surgery - the occurrence of surgery, which was not anticipated and, which was required directly because of nosocomial infection. Examples include:- debridement and resuturing of a sternal wound because of nosocomial infection; surgical insertion of a central venous line for administration of antibiotic required for the treatment of nosocomial infection.

5) readmission to the PICU because of nosocomial infection. It is recognized that this particular assessment may be open to confounding. In some instances the situation is entirely clear - for example a nosocomially infected median sternotomy wound which requires further debridement and resuturing and hence PICU admission post operatively. If it was not entirely clear whether or not PICU readmission was a direct consequence of nosocomial infection, a consensus decision by the patient's attending physician and the PICU physician was made.

6) days of antibiotic treatment for nosocomial infection. This referred to:-

a) therapy instituted for and continued for nosocomial infection.

b) therapy instituted for some other reason and then continued (because of the development of nosocomial infection) when it would otherwise have been discontinued.

The Drug Information Service in the Hospital for Sick Children, Toronto, provided an estimate of unit dose cost for each based on a 5kg. patient with normal renal and hepatic function. This included drug acquisition cost per dose plus the estimated pharmacy cost per dose. The individual weights of infected patients were used to calculate the total cost of each drug.

Figure 8 DATA COLLECTION SHEET III

Data Collection
Sheet III

Date									
PICU day no.									
Isolation									
Extra surgery									
Delay/cancel surg									
Removal device									
Antibiotic									
Antibiotic									
Antibiotic									
Antibiotic									

8.3 RESULTS

Results are presented in three sections:-
the incidence of adverse clinical events; mortality rates in infected and uninfected patients, and the antibiotic costing study.

8.3.1 Incidence of adverse clinical events

A total of 48 patients developed 100 nosocomial infections while in the PICU and as a result 20 adverse events (excluding antibiotic use) occurred. These were: 8 instances of a requirement for extra surgery; 7 instances of removal of a therapeutic device; 1 instance of delayed surgery; 1 instance of isolation; 3 instances of readmission to the PICU. Thirty six infected patients received antibiotic treatment for their nosocomial infections. Table 20 details the incidence of adverse clinical events in association with infected patients.

Table 20 Adverse clinical events in nosocomially infected patients

Event	No. patients	Notes
extra surgery	8	cardiac conduit re-do (2) sternum re-suturing (3) re-insertion PD cath. (1) surgical insertions CVL (2)
cancel/delay surgery	1	delay Switch procedure
removal of device	7	urinary catheter (1) CVL (3) arterial line (1) PD catheter (1) peripheral IV (1)
isolation	1	14 days wound/skin precautions
readmission	3	sternotomy wound infection (3)

TOTAL NO. ADVERSE EVENTS = 20

TOTAL NO. INFECTED PATIENTS = 48

8.3.2 Mortality

The overall mortality rate in the PICU was 10% (69/685) with deaths in 10% of patients without nosocomial infection (63/637) and deaths in 12.5% of patients with nosocomial infection (6/48) ($p > 0.5$).

8.3.3 Antibiotic Costing Study

The cost of individual antibiotic drugs is detailed in Table 21. Cost is based on unit dose preparation (except in the case of ampicillin and clindamycin) in a 5 Kg. patient with normal renal and hepatic function. The total cost of each antibiotic is detailed in Table 22.

Table 21 Cost of intravenous antibiotic (based on unit dose preparation).

Drug	single dose*	drug acquisition cost/dose[t]	estimated pharmacy cost/dose
amphotericin	1mg/kg=5mg	$2.88	$3.20
ampicillin	25mg/kg=125mg	$0.80	NA**
cefotaxime	50mg/kg=250mg	$3.17	$3.58
ceftazidine	50mg/kg=250mg	$3.88	$4.29
cefuroxime	25mg/kg=125mg	$0.99	$1.26
clindamycin	10mg/kg=50mg	$0.46	NA**
cloxacillin	50mg/kg=250mg	$O.47	$0.65
gentamicin	2.5mg/kg=12.5mg	$0.31	$1.99
metronidazole	10mg/kg=50mg	$0.57	$0.80
piperacillin	75mg/kg=375mg	$1.24	$1.54
ticarcillin	75mg/kg=375mg	$1.12	$1.54
tobramycin	2.5mg/kg=12.5mg	$0.73	$2.41
vancomycin	10mg/kg=50mg	$2.16	$2.49

* based on a 5kg. patient with normal renal and hepatic function.

t based on unit dose preparation. Costs would be higher with non-unit dose distribution.

** ampicillin and clindamycin are reconstituted and the doses are prepared on each nursing unit by nursing staff, not by pharmacy.

Table 22 Total cost of intravenous antibiotic for treatment of nosocomial infection*

Drug	cost/dose	no. days treatment	total cost
amphotericin	$3.20	91	$420.00
ampicillin	NA	32	$160.00
cefotaxime	$14.32	23	$2148.00
ceftazidine	$17.16	45	$9116.00
cefuroxime	$3.78	22	$165.00
clindamycin	NA	20	$246.00
cloxacillin	$2.60	88	$460.00
gentamicin	$5.97	96	$1344.00
metronidazole	$0.80	8	$12.00
piperacillin	$6.16	28	$188.00
ticarcillin	$6.16	5	$22.00
tobramycin	$7.23	12	$596.00
vancomycin	$9.96	44	$450.00
TOTAL COST			Can$15,327.00

* based on estimated pharmacy cost per dose

8.4 DISCUSSION

In this study in a Paediatric Intensive Care Unit, the adverse sequelae of nosocomial infection have been expressed in simple terms which, it is hoped, are meaningful to the practising clinician. The clinical events, whose incidence is reported in this study, were selected after consultation with PICU physicians and nursing staff who judged them to be of adverse clinical significance.

This approach has certain limitations which must be clearly understood. Firstly, data must be gathered prospectively since a knowledge and understanding of the exact clinical circumstances surrounding individual episodes of infection is mandatory before any adverse sequelae can reliably be attributed to that infection. Secondly, only a very conservative estimate of antibiotic expenditure is provided; the costing study counted only intravenous antibiotic prescribed for proven nosocomial infections. It did not include oral antibiotic (cost relatively trivial) or antibiotic prescribed empirically for 'presumed sepsis' which was discontinued after the results of a 'septic workup' showed negative.

Broadly speaking, infections produce adverse effects which can be arbitrarily separated into one of three: general discomfort, anxiety or inconvenience to patients, parents

or staff; specific detriment to the patient (or risk thereof); and increased patient care expenditure.

General discomfort, anxiety or inconvenience to patients, parents and or staff are self explanatory. For example, anticipation of extra surgery or delay in surgery caused additional stress to parents and patients, the re-siting of indwelling vascular catheters (removed because of infection) often required additional sedation or even paralysis of the child. Technical procedures themselves were, at times, remarkably time consuming for the attending staff. Equally obvious, is increased cost resulting from nosocomial infection. Surgical procedures requiring sterile operating room facilities and/or cardio-pulmonary bypass, disposable items used for isolation techniques, costly devices e.g., double lumen CVL all contribute to overall increased patient care expenditure.

Nosocomial infections cause effects, whose implications, frequently can only be assessed when the clinical circumstances are taken into consideration. For example, delay in surgery, as occurred in one patient in this study, may be extremely detrimental if there is a recognized optimum timing for a procedure and this is missed. The case in question involved a neonate with coarctation of the aorta plus transposition of the great vessels with intact ventricular septum. This infant developed a nosocomial wound infection following emergency repair of his

coarctation when a few hours old. As a result the definitive surgical procedure (arterial Switch procedure (Jatene 1976)), was delayed. There is a need for caution in advising arterial switch repair for TGA with intact ventricular septum in patients who are more than 2 weeks old. In such patients the posterior ventricle rapidly diminishes in mass shortly after birth (Lev 1969) (Tynan 1972), and becomes incapable of sustaining the systemic circulation after anatomical correction (Yacoub 1976) (British Medical Journal 1976). In our case, surgery was delayed only 10 days and fortunately arterial switch was not precluded. To our knowledge this infant suffered no deleterious effects but this was, potentially, an extremely serious sequel to a nosocomial infection.

Isolation techniques range from total isolation (separate room, gown and glove for patient contact) to skin or wound isolation only (gown and glove for patient contact). Our single case (an infant) required 14 days of skin/wound precautions for pseudomonas aeruginosa infection. Effects of this included: an absolute requirement for a 1:1 nurse:patient ratio at all times; complicated patient transfer outwith the PICU for procedures e.g., CT scan in radiology department and reduced physical contact with patients. In a recent randomized comparative trial in a PICU, Klein (1987) studied the use of gown and gloves for all patient contacts and claimed that reduced handling of

the child (e.g., patting, soothing gestures) did not occur but this was not our subjective experience.

With regard to extra surgery; apart from the inherent risk of individual procedures themselves, without exception, there was a requirement for general anaesthesia in an already compromised child. Eight patients required extra surgery; 5 were cardiac surgical patients with infected post operative wounds including 2 patients with deep mediastinitis. In 3 cases debridement and resuturing of sternotomy wound was required; in another 2 cases a total revision of an infected intra-cardiac conduit system, requiring cardiopulomonary bypass, was necessary.

Removal of a therapeutic device because of infection was indicated in 7 patients; in 3 patients a central venous line was removed and in 2 of these there was necessity for a new line to be inserted (in one case as a surgical procedure, under general anaesthesia).

Readmission to the PICU was indicated in 3 patients all of whom had acquired infection of cardiac post operative wounds during their first PICU admission. These patients required debridement and resuturing of the sternotomy wound with routine admission thereafter. In all three patients the original surgery was deemed to have been successful and unlikely to require revision, therefore, readmission (as

well as extra surgery) was due solely to nosocomial infection.

This study has demonstrated that in 48 patients who developed nosocomial infection, intravenous antibiotic costs alone were at least Can$ 15,500 (approximately £7,500). The incidence study reported in Chapter 5 reports of nosocomial infection rate of 7 infected patients per 100 patients admitted; 15 infections per 1200 patients admitted / 15 infections per 100 patients admitted. The PICU has an annual admission rate of 1,400 patients, therefore, in one year the projected cost of antibiotic for treatment of nosocomial infection would be at least Can$30,000 (£15,000). Clearly, this sum is an extremely conservative estimate. It does not include the cost of antibiotic administered because of suspicion of nosocomial infection - this was usually continued until cultures taken as part of a septic work-up were reported negative. Calculations did not take account of associated costs of drug administration e.g., IV infusion equipment, plasma drug assays for therapeutic monitoring etc.

In the incidence study described in Chapter 5, it was reported that the most frequent organisms causing nosocomial infection in this PICU were staphylococci (CONS) (30% of cases); Staphylococcus Aureus (8% of cases), Pseudomonas aeruginosa (21% of cases) and candida species (19% of cases). Accordingly, in this PICU the use of

potentially hazardous antibiotics, notably gentamicin, vancomycin and amphotericin, is often indicated. During the study period, for treatment of nosocomial infection, 6 patients received a total of 96 days treatment with gentamicin; 4 patients received a total of 44 days treatment with vancomycin; 5 patients received a total of 90 days treatment with amphotericin; 2 patients received vancomycin and amphotericin simultaneously and 1 patient received vancomycin and gentamicin simultaneously.

Nephrotoxicity has been associated with the use of vancomycin since its introduction (Waisbren 1960). Farber et al (1983) in a retrospective study of the toxicity of vancomycin preparations reported incidences of nephrotoxity of 5% when vancomycin was used alone, 10-26% when aminoglycoside was used alone and 35% when vancomycin was used in combination with an aminoglycoside. Odio (1984) has suggested that this phenomenon, known as 'synergistic toxicity', may be a problem in children though Swinney et al (1987) have disputed this fact.

Koren (1988) recently studied the pharmacokinetics and adverse effects of amphotericin B in infants and children. In his series 4 children developed serious effects (generalized pain requiring narcotic; flushing, chills and fever requiring diphenhydramine; urticaria; nausea and vomiting). Furthermore 11 patients out of 13 developed a significant reduction in serum potassium despite daily

supplementation; 6 out of 7 developed a significant increase in plasma urea and 6 out of 9 developed a significant increase in plasma creatinine. Recurrent hypokalaemia was certainly noted in many of our patients who were receiving amphotericin though this was not formally studied.

It is recommended that because of the large pharmacokinetic variability and the high rate of serious adverse effects, individualized dosing of amphotericin B based on therapeutic drug monitoring should be performed (Koren 1988). Likewise drug monitoring is mandatory when using gentamicin and vancomycin. Drug assays such as these performed perhaps every other day, certainly add to the overall cost of the antibiotic treatment, though this study did not seek to quantify this aspect.

Vancomycin and amphotericin have other significant disadvantages; intravenous administration of these drugs is irritant to veins (and may ultimately require use of a central venous line); both drugs require dilution in a relatively large volume of fluid which, in the small child, may constitute almost the entire fluid allowance for 24 hours, and preclude administration of other 'useful' fluids e.g., parenteral nutrition.

As discussed previously, prolongation of stay and increased cost secondary to nosocomial infection may be estimated by

means of a matched cohort study (see Section 1.5.4) though studies in adult patients have been beset by difficulties finding adequate numbers of matched 'control' patients. It may be assumed that in the PICU, because of the wide range of pathology and age related response to illness, the tasks would be even more onerous and for this reason, it was decided not to attempt a formal matched cohort study nor to attempt subjective, physician-based estimation of prolongation of PICU stay.

With regard to mortality; the relationship between mortality; severity of underlying illness and development of nosocomial infection is discussed in Chapter 5 of this volume. In this survey, mortality rates in infected and uninfected patients did not vary significantly and it is suggested that nosocomial infection rate does not increase mortality though the power to detect a difference is low.

CHAPTER 9

SUMMARY AND GENERAL CONCLUSIONS

SUMMARY AND GENERAL CONCLUSIONS

The following summarises the principal findings and conclusions drawn from results of the studies described in the previous section.

The Present

This survey reports an overall nosocomial infection rate of 7 infected patients per 100 admissions (or 14.6 infections per 100 admissions), over a period of eight months, and in a population characterized by underlying severity of illness, in the PICU, Hospital for Sick Children, Toronto. The commonest infecting organisms are coagulase negative staphylococci, Pseudomonas aeruginosa, Candida species and Staphylococcus aureus. The commonest sites of infection are blood stream, skin/eye/wound; respiratory tract and urinary tract.

With regard to cardiac surgery patients; the common causative agents in wound infections following closed (non bypass) cases are Staphylococcus aureus and coagulase negative staphylococci. Following open (bypass) cases wound infections are caused most frequently by coagulase negative staphylococci, Pseudomonas aeruginosa, Candida species and Staphylococcus aureus. Overall, non-wound infections account for 72% of total infections.

In this PICU, nosocomial infection creates a significant burden of illness - physical, emotional and financial, which is ultimately borne by the patients, by their families and by the institution. The study confirms that certain events (considered to be of adverse clinical significance either because of anxiety/discomfort/ inconvenience to patients/parents/staff or because of increased cost) occur in up to 40% of infected patients. Nosocomially infected patients invariably require antibiotic treatment. The minimum drug cost for 100 nosocomially acquired infections is $15,000. Mortality rates do not appear to be significantly increased as a result of nosocomial infection.

There is no doubt that the era of unlimited medical resources has ended. In the United States, for example, the cost of health care has increased more rapidly than the rate of inflation (Freeland 1980). Patients in critical care units consume a disproportionate quantity of hospital resources, especially paradoxically, those patients with the poorest prognosis for survival (Cullen 1984) (Schroeder 1981) (Detsky 1981) (Scheffler 1982).

As discussed in the introduction to this thesis, if the burden of illness created by nosocomial infection in paediatric intensive care units is to be reduced, two crucially important issues must be addressed namely;

predisposing risk factors and efficient infection surveillance strategies.

Risk factors for the acquisition of infection have to be identified in order to guide allocation of resources in infection control and focus future research efforts. In study populations, predisposing risks have to be clearly understood before the efficacy of any particular intervention strategy can be assessed. Interventions themselves may be expensive and to be cost-effective may need to be applied selectively to targeted cases, considered to be at risk of infection.

Efficient infection surveillance strategies must be devised in order to identify infection accurately and rapidly thereby reducing the use of unnecessary antibiotic therapy yet averting the progression to life threatening sepsis. To be practicable, surveillance strategies must be suitable for day to day use in a busy PICU where there are, inevitably, limitations on available Infection Control Staff time.

This study demonstrates that severity of underlying illness, as measured by the PRISM scoring system, predicts a population in the PICU who are at risk of developing nosocomial infection. Patients with an admission PRISM score of ≥ 10 are significantly more likely to acquire infection than those with scores <10 (10.8% vs 3.6%,

$p<0.001$). In cardiac surgery patients additional risk factors for acquisition of infection may be identified. These relate to certain surgical procedures and specific surgical techniques namely an 'open' sternum in the immediate post operative period. It is particularly advantageous that using these markers patients may be stratified by risk from the moment of admission hence intervention strategies applied from the outset of their stay.

With regard to an effective nosocomial infection surveillance strategy; the sensitivity of the system of surveillance recently introduced for routine use in the PICU, (the Infection Control Sentinel Sheet (ICSS)), has been found to compare very favourably with daily bedside examination of patients plus chart review. The ICSS system requires only 20 minutes of surveillance time per day and detects: 87% of nosocomially infected patients; 85% of infections at the three standard sites (blood, wound and urine); and 72% of infections at all 11 sites surveyed. Following this study, it is intended to make some minor adjustments to the system to improve its sensitivity.

The Future

During the last decade researchers in adult critical care units have identified a variety of infection control techniques and future research efforts have been focussed.

These techniques can be variably applied to the situation in the PICU since the distribution of infection within these two units differs. In the light of the findings of this study, some of the current innovations in nosocomial infection control in critical care units will be reviewed and areas where future research should be directed will be identified.

As a general statement, there is a requirement to devise and evaluate strategies which block transmission of organisms between patients and which prevent, or at least delay, nosocomial colonization. The use of simple barrier precautions warrants further study. Some workers have demonstrated the use of protective isolation to be useless (Donowitz 1986a) (Preston 1980) though Leclaire et al (1987) recently showed that routine use of gown and gloves in a paediatric unit significantly reduced the incidence of endemic respiratory syncitial virus infection Klein (1987) found in a 2 1/2 year prospective randomized comparative trial in a PICU that the use of disposable, nonwoven polypropylene gowns and latex gloves for all patient contacts reduced the incidence of nosocomial infections two fold.

In this PICU, skin/eye/drain site infections account for 22% of the total and wound infections for 15% of the total. More studies of cutaneous antiseptics (used for hand washing, intravascular line site care and patient bathing)

are needed with infection rather than colonization as the index of comparison.

Vascular line related infections account for 24% of the total infections and catheter associated urinary tract infections for 9% of the total. There is considerable evidence that the material used in construction of a device for implantation is an important determinant in whether there is an attractive surface for adherence of pathogenic micro-organisms. (Ashkenazi 1984) (Gristina 1987). Current research efforts are being directed towards new designs which reduce colonization of surface polymers and the development of non thrombogenic, colonization resistant polymers possibly incorporating antimicrobials onto surfaces or onto the polyer itself. (Trooskin 1985) (Schaeffer 1988) (Maki 1987). The addition of non toxic biodegradable antiseptics to intravenous fluids is another possibility. (Freeman 1982).

This study reports that lower respiratory tract infections account for 10% of total infections. In adult ICU patients, where the incidence of nosocomial pneumonia is considerably greater, there is little evidence that significant progress is being made in either its prevention or its treatment. More information is needed on the effects of gastric colonization, the frequency of gastric reflux and the role of the nasogastric tube as a risk factor.

It is suggested that oral and gastrointestinal tract decontamination with topical, non-absorbable antibiotics prevents nosocomial respiratory infection in ICU patients (Stoutenbeek 1987) (Unertl 1987) (Ledingham 1988) though epidemiologically, the long term results of such a policy are unclear. Driks et al (1987) recently have demonstrated that the use of a 'cryoprotective' gastric barrier agent (sucralfate) which preserves the natural gastric barriers against bacterial overgrowth), rather than antacids or H_2 antagonists for stress prophylaxis, reduced the incidence of nosocomial pneumonia two fold. In vitro data presented by Daschner (1988) and Tryba et al (1987) suggests that sucralfate may also have an intrinsic antibacterial effect against gram negative bacilli that is greater than that observed with gastric acid. At the present time, neither of these techniques has been assessed in paediatric patients.

The increased use of diagnostic tests has substantially heightened awareness of infectious disease. However, there continues to be a substantial need for reliable methods of distinguishing colonization from infection, particularly in the lower respiratory tract.

Despite efforts in most PICUs to develop antibiotic policies, usage of antimicrobials is still not optimal. Pressure of use of antibiotic exerts a powerful influence on the microbiological status of the hospital generally and

on the profile of PICU nosocomial infection in particular. Modern day ICUs are spawning grounds for the so called 'Andromeda' strains of multiply resistant bacteria that are now being encountered throughout the world (Crichton 1982). Furthermore, it is concerning that candida species seem to be on the increase as pathogens - in this PICU candida accounts for 20% of infections. Future studies should aim to define the factors governing superinfection by resistant bacteria and candida.

Finally, the most important infection control measure yet the oldest and probably the cheapest - handwashing, continues to be performed inconsistently by all health care personnel and, sadly, the greatest offenders, in this respect, are physicians. In terms of infection control, a change in attitude towards this simple issue would result in vast immediate benefits.

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PUBLICATIONS

The following publications resulted from the work described in this thesis and are at present in press.

1. Evaluation of a new method of detection of nosocomial infection in the Pediatric Intensive Care Unit: The Infection Control Sentinel Sheet System.
   EL Ford-Jones, CM Mindorff, E Pollock et al.
   Infection Control and Hospital Epidemiology 1989; 10: 515-520.

2. Early nosocomial infections in pediatric cardiovascular surgery patients.
   E Pollock, EL Ford-Jones, I Rebeyka et al.
   Critical Care Medicine - in press 1989.

APPENDIX 1

HOSPITAL FOR SICK CHILDREN, TORONTO
Infection Control Policies for Physicians and Surgeons

Hands must be washed for 15 seconds by the clock before and after patient contacts (or between patient contacts if you are touching charts, leaning on cribs etc. between patients) or if going from a dirty area such as a wound to a clean area such as the eyes. This will remove all organisms transiently adhering to the skin.
(True emergencies are excepted of course).

CAREFUL THOROUGH HANDWASHING IS THE MOST IMPORTANT SINGLE PROCEDURE IN PREVENTING THE SPREAD OF NOSOCOMIAL INFECTIONS

Dermatitis which predisposes to permanent carriage of pathogens is to be prevented through the use of single use packets of hand lotion. Multi-use bottles have been identified as reservoirs of pathogens during epidemics.

Gowns are to be changed before and after contact with patients in isolation. When removing gowns, if gloves are not worn, carefully untie the ties and remove the gown by the cuffs, causing a minimum of air disturbance. Wash hands for 15 seconds. When removing gowns, if gloves are worn, carefully untie the ties and remove the gown by the cuffs, causing a minimum of air disturbance. Remove gloves "rubber to rubber and skin to skin". Wash hands for 15 seconds. Patients with any symptoms of infection are to be isolated promptly on identification of symptoms compatible with diseases listed in the yellow pages of the Infection Control Manual.

Skin Preparation for an invasive procedure - intravenous infusion, arterial line, blood culture in any patient or <u>any</u> procedure in an immunodeficient patient.

(1) if the skin is not clean, it must be cleaned mechanically with isopropyl alcohol 70% by a doctor or nurse who has just washed his or her hands.
(2) the appropriate antiseptic is chosen.
(3) after any dirt or blood on the skin has been removed by cleansing, the appropriate antiseptic is applied liberally, using friction, working from the centre of the field to the periphery.
(4) the antiseptic must be allowed to dry for 30 seconds (povidone-iodine) or 60 seconds (alcohol). No antiseptic works immediately.
(5) if povidone-iodine has been used and allowed to dry and the insertion site is to be palpated, the finger doing the palpation must also undergo skin preparation as in 4 above. (alternatively sterile gloves may be worn).

Skin Preparation for blood sampling other than blood cultures

(1) the skin is cleaned with isopropyl alcohol 70%.
(2) the antiseptic is allowed to dry (30 to 60 seconds).

Note

Because there is usually no indwelling device and the patient is not immunodeficient there is usually no need for the more thorough skin preparation in such cases.

Prevention of Intravascular Infections (occult bacteraemia, septic thrombophlebitis, cellulitis)

(a) IV cannulae should be used only when indicated and discontinued when no longer indicated.
(b) Use measures aimed at preventing contamination of the insertion site during insertion:-
thorough handwashing prior to insertion,
scrub site with antiseptic (Betadine) for 30-60 seconds,
secure cannula to stabilise it,
apply sterile dressing (gauze, bandaid, Tegederm, Opsite) to skin catheter junction,
(c) Change intravenous catheters at 72 hours. Beyond this time the risk of bacteraemia increases from 5% to 8%.

ALL INTRAVASCULAR LINES ARE DATED TO REMIND STAFF THAT THE RISK OF ASSOCIATED INFECTION IS RELATED TO THE TIME LEFT IN PLACE.

Urinary tract catheterisation

For short term use - 2 or 3 single catheterisations over 48 - 72 hours presents a lower infection risk than indwelling catheterisation. Alternatives include condom drainage (Texas catheter). See procedure on page 115 of the H.S.C. Infection Control Manual which stresses the importance of a closed, freely draining system opened only by personnel familiar with this policy. (Wash hands, wear gloves, cleanse perineum with iodophor, use lubricated catheter). Remove as soon as possible.

Collection of blood for blood cultures

Wipe the diaphragm tops of the culture bottles with 70% isopropyl alcohol and leave the alcohol wipe in place on the blood culture bottle. If the skin is dirty, clean it with 70% isopropyl alcohol and allow to dry. This removes any dirt or blood on the skin that may interfere with disinfection. See Skin Preparation (p 102) for details. Swab the site with 10% povidone-iodine concentrically. Allow to dry (about 60 seconds). Alternatively wear sterile gloves. Change the needle on the syringe before transferring the blood to the blood culture bottle. Blood

cultures must be inoculated before any other collection tubes. Pseudomonas fluorescens is a contaminant found in coagulation study (citrate) tubes. If an additional skin puncture is required, use a new needle. Dispose of all discarded needles in a sharps container. Visitors are screened for the presence of skin or respiratory infections. Simple handwashing is sufficient and long sleeved gowns are worn. A visitor should receive strict instructions to handle only his or her child and not to touch equipment or surfaces used for other patients. Visitors under 12 are not permitted except in consultation with the nurse in charge.

If you have an infection and must continue to work, please observe the following:
If you have diarrhoea - wash hands very carefully after using the bathroom and before touching patients or their equipment. Try to avoid working with patients with metabolic disease.

If you have a cold or any other respiratory infection, try to avoid working when acutely ill, wear mask and gown for any direct contact with patients (especially infants, patients with congenital heart disease and immune suppressed patients) and wash hands thoroughly before touching patients and their equipment. 70% or more of personnel with colds have the virus on their hands.

If you have a cold sore which is not completely dry you should not work with neonates or with patients who have burns, immuno-deficiency, blood dyscrasias or skin disorders. If it is essential that you work cover the cold sore with a mask or bandaid and wash hands thoroughly before touching any patient. 60% or more of patients with cold sores have the virus on their hands. If you have herpetic whitlow (cold sore on the finger) you should not have direct patient contact until the lesion is dry. If you have a constant pain in one area, watch carefully to be sure that shingles are not developing.

If you have any other infections, including abscesses or boils please check with Occupational Health (daytime) or Infectious Diseases (nights and weekends) before working.

If you are exposed to chickenpox and have never had chickenpox, lived in the same house with or cared for someone with chickenpox, please check with Occupational Health to determine if and when you should go on leave of absence. If you are exposed to measles please notfy Occupational Health (daytime) or Infectious Diseases (nights and weekends) before working.

If you are exposed to blood through contact with mucosa, eye, or have massive skin contact, please consult Occupational Health to assess the need for Hepatitis B prophylaxis.

If you are exposed to whooping cough, and develop a cough, remind your doctor to consider that you may have whooping cough. Reportable disease listed on p 90 of the HSC Infection Control Manual, must be reported. This is the physician's responsibility.

APPENDIX 2

Management of intravascular lines; solution, tubing and dressing changes

Types of Dressing

arterial line
site is cleaned with povidone iodine; sterile elastoplast bandages are applied one under the catheter hub and one over the insertion site.

central venous line
semipermeable dressing (Uniflex(R)) is used in normal circumstances.

Gauze dressing is used when:-
frequent observation of the site is required,
the site and/or surrounding areas are infected,
a topical cream or ointment is prescribed,
the patient is diaphoretic and transparent dressings are not sufficiently adhesive.

PERIPHERAL INTRAVENOUS INFUSIONS

Regular IV solutions

bag/syringe	-	every 24 hours + prn + at tubing change,
tubing	-	every 48 hours includes T piece,

TPN

bag/syringe	-	every 24 hours + prn + at tube change,
tubing	-	every 48 hours includes T piece,
med line Y connected	-	every 48 hours,
Dressing/Tapes	-	prn.

ICU CVP LINES

Regular IV solutions

bag/syringe	-	every 24 hours + prn + at tubing change,

TPN

bag/syringe	-	every 24 hours + prn + at tubing change,
tubing	-	every 72 hours includes T piece,
med line Y connected in	-	every 72 hours,

Dressing

(semipermeable)	-	every 7 days and prn,
(gauze)	-	every day if there is an infection or if ointment is prescribed, otherwise every 3 days.

LIFE LINES / WB CATHETERS

Regular IV solutions

bag/syringe	-	every 24 hours + prn + at tubing change,
tubing	-	every 48 hours includes T piece,

TPN

bag/syringe	-	every 24 hours + prn + at tubing change,
tubing	-	every 72 hours includes T piece,
med line Y connected in	-	every 72 hours.

Dressing - every 7 days and prn,

ARTERIAL LINES

syringe	-	every 24 hours and at tubing change,
tubing	-	every 48 hours,
pressure tubing/ transducer	-	consider at day 10.

Dressing
on day 4 and every 3rd day thereafter or prn by nurse at charge level. On catheter day 10 the site is evaulated by the medical staff and consideration is given to changing the tubing and catheter site.

TRANSTHORACIC LINE (eg RA, LA, PA)

syringe	-	every 24 hours + prn + at tubing change,
tubing	-	every 48 hours,
pressure tubing/ transducer	-	consider at day 10.

BLOOD TUBING

blood product	-	every 6 hours,
tubing	-	every 24 hours (if blood in tubing >6 hours old, flush tubing through with new bag hung), (if blood warmer in use change tubing and bag every 4 hours).

APPENDIX 3

Nursing care of post operative cardiac surgery patients: incision, chest tube, pacing wires and transthoracic lines in the post-op cardiovascular patient in ICU.

Note
Surgihesive ((R) Squibb) is a sterile waterproof bandage. Opsite is a transparent semipermeable dressing.

INCISION

Operating Room	surgihesive
Initial Care	assess dressing and change if not intact or saturated with blood.
Day 3	dressing is changed and op-site is applied.
Continuing Care	transfer to ward or on day 7 remove op-site and discontinue dressing if clean and dry.

CHEST TUBE

Operating Room	surgihesive
Initial Care	assess dressing and change if not intact or saturated with blood.
Day 3	dressing is changed and an elastoplast dressing applied.
Continuing Care	dressing change every 3 days.

PACING WIRES

Operating Room	no dressing.
Initial Care	dress after 1st post-op bath, elastoplast applied.
Day 3	dressing change.
Continuing Care	dressing change every 3 days.

TRANSTHORACIC LINES

Operating Room	no dressing.
Initial Care	post bath clean exit site with a betadine swab. Remove betadine with sterile water.
Day 3)	clean exit sites as described
Continuing Care)	following each bath until removed.

Note
It is the responsibility of the bed side nurse to ensure sterile scissors are available for chest tube removal.

Special Considerations
Follow the procedure for a sterile dressing change as outlined in the HSC Nursing Procedure Manual. Remove betadine with sterile water before applying your sterile dressings. Use sterile scissors to cut elastoplast dressings for chest tubes and pacing wires.

APPENDIX 4

Care of Ventilated Patients

All patients are ventilated using either volume or pressure limited ventilators, usually via a nasal endotracheal tube. Endotracheal tubes are routinely suctioned hourly (more frequently if required in invidual circumstances), using a sterile, 'no touch' technique. Ventilator tubing is changed every 3 days unless the endotracheal tube secretions are heavily contaminated with a known pathogen, in which case the tubing is changed daily.
Sterile water in humidifier circuits is changed daily.

APPENDIX 5

Nursing care procedure - prevention of nosocomial conjunctivitis

Conjunctivitis is a common childhood illness that may range from a mild self-limited infection to one that can destroy vision and even cause death. Conjunctivitis caused by gram negative enteric bacteria (usually P aeruginosa) may lead to rapidly progressive and destructive ocular disease. Other common pathogens that may lead to eye damage or blindness are Haemophilus Influenzae, Strepthococcus pneumoniae, Staphylococcus aureus, Branhamella Catarrhalis, and Neisseria meningitides. The risk of contaminating the cornea with nasopharyngeal secretions is directly related to interventions such as intubation, tracheotomy care and suctioning, administration of oxygen by hood or administration of oxygen / air by croupette.

Usual Problems/Objectives/Timing

1. Potential contamination of the cornea with nasopharyngeal or endotracheal secretions.

a) Be aware of procedures / interventions that may put the patient at risk for corneal contamination. For example:
   - suctioning an ET tube or tracheotomy tube.
   - manipulation of a nasogastric tube.
   - use of an oxygen hood or croupette (where condensation forms and moisture drops on the patient's face).
   - colonization of pathogens.

b) Ensure that fluid and debris does not fall from equipment onto the patient's face when suctioning or administering tube feedings. Always withdraw the tube away from (not over) the patient's face.

c) Cover the patient's eyes with a tissue when suctioning.

d) If necessary, enlist a second person to help restrain the patient's head when carrying out procedures such as suctioning.

e) Maintain an oxygen hood and croupette only for as long as ordered.

2. Potential delay in identifying and treating conjunctivitis.

a) Observe patient's eyes for redness and presence of serous or purulent drainage.

b) If there is any redness or discharge from the eye(s), send a swab for culture and sensitivities stat (prompt identification of the causative organisms is essential): simultaneously, notify the doctor and obtain orders.

c) Document the condition of the eye and action taken in the pateint's progress notes.

3. If conjunctivitis is diagnosed. Potential, progressive and destructive ocular disease due to incorrect management of procedures and poor hygiene.

a) Using sterile cotton swabs and sterile water, cleanse the patient's eyes every 4 hours and p.r.n.

b) Record the condition of the patient's eyes before cleansing, noting any drainage (amount and type), the procedure and the condition of the eye afterwards.

c) Ensure that a freshly opened container of sterile water is used for each procedure (do not leave containers at the bedside).

d) Instruct the patient not to rub the eyes (arm restraints may be necessary for an infant or young child).

e) Explain to the family the importance of washing hands before and after handling the child and not to use washcloth or towel to wipe the eyes (some forms of conjunctivitis are highly contagious).

f) Change linen frequently, especially the pillow case, washcloth and towel.

APPENDIX 6

Definition of Closed and Open Cardiac Surgery

CLOSED	OPEN
Closure of sternum	Repair of ASD
Ligation of PDA	Repair of VSD
Embolectomy	Repair of AVSD
Pacemaker Insertion	Repair of Tetralogy of Fallot
Glenn anastomosis	Arterial or Switch repair
Blalock Taussig shunt	Mustard procedure
Blalock Hanlon shunt	Valve replacement
Central shunt	Rastelli procedure
Coarctation of aorta repair	Fontan procedure
Double aortic arch repair	Repair of double outlet Right ventricle
Innominate artery suspension	
Mitral/aortic/pulmonary valvotomy	
Pulmonary artery banding	Konno procedure
Insertion of pericardial drain	Bertall procedure
	Repair of total or partial anomalous venous drainage
	Repair of sub-aortic stenosis
	Repair of truncus arteriosus
	Mapping for WPW syndrome
	Norwood procedure